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The American Heart Journal

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Original Communications

MYOCARDITIS*

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In hearts showing the different types of cardiac failure, areas of fibrosis of varying degrees may not infrequently be found. There is a difference of opinion concerning the origin of these fibrotic areas. Some observers consider them to be the result of inflammation, while others look upon a greater part of the fibrosis as a result of myocardial anemia following a narrowing of the coronary arteries.

Cardiac failure with essential hypertension, old valve defects, coronary sclerosis, coronary thrombosis, toxic myocardium, and syphilitic aortitis is commonly diagnosed acute or chronic myocarditis without regard to the pathological condition of the heart.

The purpose of this paper is to study the character, origin, frequency, extent, and result of the myocardial injuries manifested anatomically in the various forms of cardiac failure in order to determine whether clinically a diagnosis of acute or chronic myocarditis should be made.

In studying these hearts the term myocarditis is used only where an inflammatory process in the heart muscle is made evident by an exudative or proliferative cellular reaction.

MATERIAL

A detailed gross and microscopical study of the myocardium was made in 429 cases of cardiac failure. The following outline shows the usual conditions which result in cardiac failure and the number of cases studied:

	cases
A. Endocarditis	
1. Acute rheumatic	30
2. Recurrent rheumatic	20
3. Subacute bacterial	60
4. Old valve defects	68
5. Syphilitic aortitis, most cases of which show endocarditis	106
B. Adherent pericardium	2
C. Right ventricular hypertrophy and dilatation	4
D. Essential hypertension	139

*From the Department of Pathology, University of Minnesota, Minneapolis, Minn. Read in abstract before the American Heart Association at Minneapolis, June 12, 1928.

Thirty-seven of the hypertensive hearts are in the group in which death occurred suddenly from a narrowing or thrombosis of the coronary arteries. On the average, about 75 per cent of all patients dying from coronary sclerosis have a high blood pressure, as indicated by the clinical history or by the size of the heart observed at necropsy. The non-hypertensive cases with coronary sclerosis show a condition in the myocardium similar in all respects to that found in the myocardium in the cases with high blood pressure, with the exception of hypertrophy.

The myocardium was examined for gross and microscopical evidences of inflammation and fibrosis. The extent of narrowing of the coronary arteries from intimal thickening was carefully noted, especially in the cases in which clinically there were symptoms of coronary disease. Five blocks from various places in the myocardium were studied in each case. Much attention was given to the type and degree of inflammation, whether it was exudative or proliferative in character, or arranged in localized areas to form abscesses or Aschoff bodies. Diffuse exudative or proliferative inflammation was also carefully looked for. The condition of the myocardium immediately surrounding the medium-sized blood vessels was carefully studied to determine whether or not peri-arterial scars were present. Such scars are commonly found in hearts in which there has been a previous rheumatic inflammation. It has been pointed out by various observers that the rheumatic inflammation generally occurs near, and often surrounding, blood vessels. When healed, the area about these vessels remains in the form of scars similar to those resulting from proliferative inflammation in heart valves or in any other part of the body.

The material studied in this paper can be placed in two groups. The first group includes the cases which result from inflammation, such as the various types of endocarditis (rheumatic, bacterial, and syphilitic) and the adherent pericardium. The second group includes the cases of cardiac failure following increased blood pressure, either systemic or pulmonary, and the cases where death resulted from a narrowing of the coronary arteries.

A detailed description of the myocardium in the various conditions associated with cardiac failure is given under the following headings:

Acute Rheumatic Endocarditis.—Death immediately associated with acute rheumatic fever is of infrequent occurrence and for that reason the study of the myocardium in a large series has not been made. It is evident, however, that this is one of the conditions in which acute myocarditis is found. Table I shows the type and frequency of inflammation in the 30 cases of acute rheumatic endocarditis which came to necropsy. It is seen that the Aschoff body is one of the outstanding evidences of inflammation. The Aschoff nodule is a localized area of inflammation mostly proliferative in character; but at times poly-

TABLE I

THE MYOCARDIUM IN ENDOCARDITIS

KIND	NO.	ASCHOFF BODIES		IRREGULAR PROLIFERATIVE INFLAMMATION		ABSCESSES		ACTIVE INFLAMMATION		PERIARTERIAL SCARS		TOTAL EVIDENCE OF INFLAMMATION, ACTIVE OR HEALED	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Acute rheumatic	30	21	70	18	60	2	6.5	24	80	–	–	24	80
Recurrent rheumatic	20	12	60	12	60	–	–	13	65	–	–	13	65
Subacute bacterial	60	27	45	36	60	13	21.5	44	73.5	38	63.5	53	88.5
Old valve defect	68	9	13	14	20.5	0	0	15	22	36	53	36	53

morphonuclear leucocytes, lymphocytes, plasma cells, and eosinophiles in varying numbers are present. The anatomy of these nodules has been described by Aschoff,[1] Geipel,[2] Coombs,[3] Fraenkel[4] and others. By many these nodules are considered specific for the virus producing rheumatic fever. This, as is shown later in studying other types of cardiac disease, does not appear always to be the case. The Aschoff bodies in varying numbers and varieties are present in 21 (70 per cent) of the 30 cases of acute rheumatic endocarditis. Fraenkel,[4] one of the earliest observers of the Aschoff nodules, found them present in the myocardium in 17 (85 per cent) of 20 cases examined. Libman[5] found them in 18 (32 per cent) of 56 cases and Thayer[6] in 22 (88 per cent) of 25 cases.

In 18 (60 per cent) of the 30 cases studied in this paper there was an irregular proliferative inflammation with a cellular reaction similar to that found in the Aschoff nodule. This type of inflammation occurs as a rule in the interstitial tissues, as does the Aschoff body. Various forms of large, elongated, irregular mononuclear and multinucleated cells having vesicular nuclei and basophilic cytoplasm are found in this diffuse and irregularly arranged proliferative inflammation. Cellular exudates similar to those found in the Aschoff bodies are also commonly present.

Abscesses as a rule are rare in the myocardium in cases of acute rheumatic endocarditis. In one of the 7 cases studied, Geipel[2] found abscesses and considered their presence the result of a secondary infection with staphylococci, although he does not report detecting these organisms by either staining or cultural methods. Abscesses as well as Aschoff nodules in large numbers were present in 2 (6.5 per cent) of the 30 cases. These two cases were typical clinical and anatomical examples of acute rheumatic endocarditis with pericarditis.

Active inflammation indicated by Aschoff bodies, irregular proliferative inflammation, or abscesses was present in 24 (80 per cent) of the 30 cases of acute rheumatic endocarditis.

Myocarditis, acute in character, is of common occurrence in cases of acute rheumatic endocarditis. The myocarditis shows a great tendency to surround vessels. It is generally proliferative in character and may leave areas of myocardial fibrosis, the extent of which may be determined by studying the myocardium in cases of old valve defect. The acute myocarditis may be at times so extensive as to be considered a factor in bringing about myocardial failure, but it evidently is not of great importance in producing cardiac failure, since death so seldom occurs in acute rheumatic endocarditis. Death immediately associated with acute rheumatic fever comprises only about 2 per cent of the total cardiac failures.

Recurrent Rheumatic Endocarditis.—This group includes cases which have had repeated attacks of acute rheumatic endocarditis and at

necropsy show the verrucous rheumatic vegetations upon previously thickened valves.

The frequency of acute myocarditis in the 20 cases of recurrent rheumatic endocarditis in the series is shown in Table I. The types and character of inflammation are similar to those found in the cases of acute rheumatic endocarditis. Abscesses, however, are not found. Active inflammation, present in 13 (65 per cent) of the 20 cases, is slightly less frequent in the recurrent than in the acute rheumatic cases.

Fig. 1.—A peri-arterial scar showing the cellular remains of a proliferative inflammation.

Subacute Bacterial Endocarditis.—The frequency and character of active inflammation and its end-result, the scar, are shown in Table I. It is not the purpose of this paper to enter into a discussion of the etiology of rheumatic fever, yet it is of interest to observe the similarity of the type of reaction found in the myocardium in acute rheumatic endocarditis to that in subacute bacterial endocarditis and the relative frequency of this inflammation in both cases. It appears from Table I that the character of the inflammation found in the myocardium cannot be used absolutely as a means of differentiation between acute rheumatic endocarditis and subacute bacterial endocarditis.

In the 60 cases of subacute bacterial endocarditis in which the myocardium was studied, Aschoff nodules were present in varying numbers in 27 (45 per cent). Often they would not have been detected if several sections had not been carefully examined. Irregular proliferative inflammation was present in 36 (60 per cent).

One outstanding point to be noted in the myocardium in cases of subacute bacterial endocarditis is the high percentage of abscesses. They are found in 13 (21.5 per cent) of the 60 cases examined. The greater frequency of abscesses in subacute bacterial endocarditis than in other forms of endocarditis evidently results from the lodging in the myocardium of infected emboli from the valves.

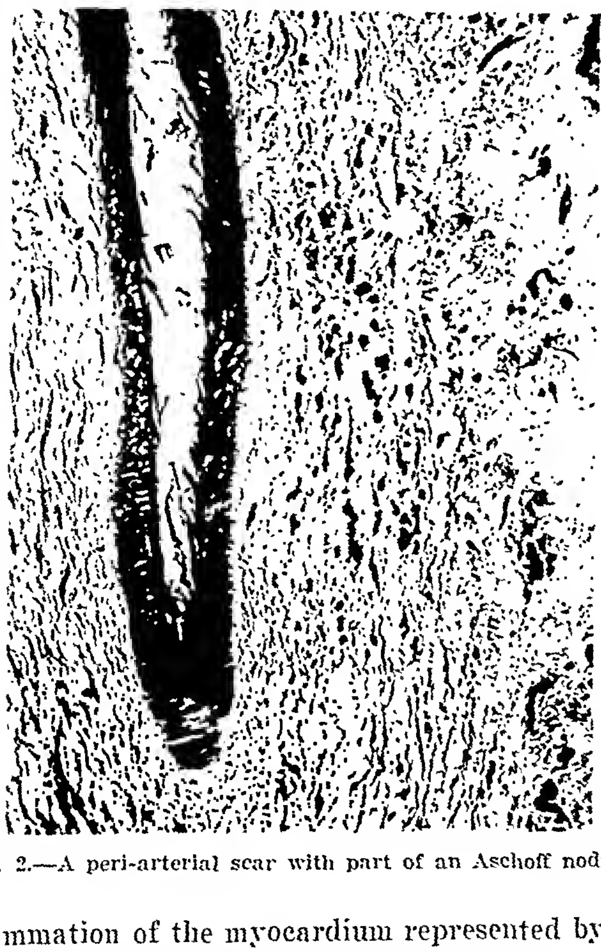

Fig. 2.—A peri-arterial scar with part of an Aschoff nodule.

Active inflammation of the myocardium represented by one or more of the described types was present in 44 (73.5 per cent) of the 60 cases. This frequency compares well with that found in acute rheumatic endocarditis. The type of scar in the myocardium in subacute bacterial endocarditis is characteristic. It is located for the most part immediately around the medium- and small-sized blood vessels and is spoken of as peri-arterial fibrosis. In most cases cellular remains of proliferative inflammation can be seen (Fig. 1). It is not uncommon to find Aschoff nodules or parts of nodules within the scars (Fig. 2). The remaining cells of these nodules have laid down collagenous fibers.

The scar is obviously the result of rheumatic peri-arterial inflammation either in diffuse or nodular arrangement. Such scars never become severe but are large enough to indicate a previous peri-arterial infection. They differ from the scar associated with coronary disease in showing a more definite and immediate relation to the blood vessels and in most cases in showing some cellular proliferative or exudative reaction. These inflammatory scars are rarely seen in the myocardium in acute rheumatic endocarditis, since apparently the inflammation has not had time to form scars, but appears as active peri-arterial inflammation. The fate of the Aschoff nodule and the diffuse rheu-

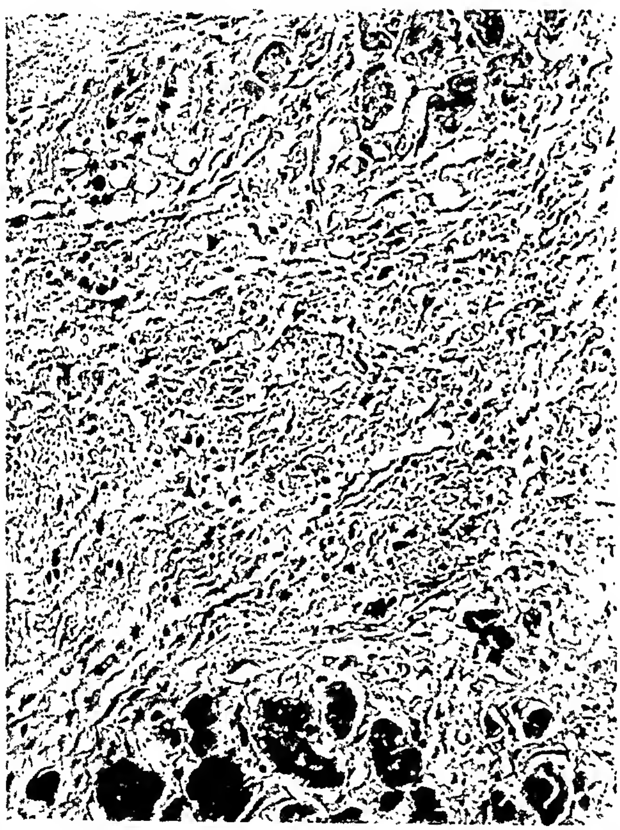

Fig. 3.—A scar from atrophy of muscle fibers with replacement by connective tissue.

matic proliferative inflammation upon healing is to form scars generally peri-arterial in arrangement and as a rule not very extensive.

The peri-arterial scar indicating a previous peri-arterial myocarditis is especially conspicuous in the myocardium in cases of subacute bacterial endocarditis. All transition stages may be seen from the active peri-arterial myocarditis, often containing Aschoff bodies, to the fully formed peri-arterial scars. These scars were found in 38 (63.5 per cent) of the 60 cases examined.

Evidence of inflammation, either active or healed, was found in 53 (88.5 per cent) of the 60 cases. It is to be noticed that myocarditis is even more frequent in subacute bacterial endocarditis than in acute

or recurrent rheumatic endocarditis. It seems reasonable that this should be so since an active infection is present over a longer period of time. Real chronic myocarditis is found in the myocardium in cases of subacute bacterial endocarditis in a higher percentage than in any other cardiac condition which we have observed. The injury to the myocardium in many cases of subacute bacterial endocarditis is to be considered a factor in the cardiac failure.

Old Valve Defects.—The frequency and types of myocardial inflammation in 68 cases where death resulted from old valve defects are shown in Table I. The Aschoff nodule was found 9 times (13 per cent). In 14 (20.5 per cent) there was irregular proliferative inflammation. Abscesses were not found in any. Active inflammation including all types was present in 15 (22 per cent). Peri-arterial scars, indicating a healed peri-arterial inflammation, were seen 36 times (53 per cent). It is to be noted that the scars are not as frequent as in the cases with subacute bacterial endocarditis. An active inflammation probably was not present over as long a period of time.

Evidence of inflammation, active or healed, was present in 36 (53 per cent) of the 68 cases. Except in one case the extent of this inflammation and fibrosis was slight and apparently had had little or no influence in bringing about the cardiac failure. The degree of coronary sclerosis was so slight, when present at all, that it appears evident that the myocardial fibrosis did not result from narrowing of the coronary arteries as it so commonly does in patients dying from coronary sclerosis.

In summarizing the facts concerning the injury found in the myocardium in the various forms of rheumatic and bacterial valvular diseases, it may be said that acute myocarditis is of common occurrence in acute rheumatic endocarditis (80 per cent), in recurrent rheumatic endocarditis (65 per cent), and in subacute bacterial endocarditis (73.5 per cent); but that it is most common in the acute rheumatic form. Acute myocarditis is only relatively frequent in cases of cardiac failure from old valve defects (22 per cent). Chronic myocarditis in the form of the peri-arterial scar occurs commonly in cases of subacute bacterial endocarditis (61.5 per cent) and in cases of old valve defects (53 per cent). Evidence of myocarditis, acute or chronic, is found more frequently in subacute bacterial endocarditis than in any other form of cardiac failure (88.5 per cent). The relative frequency of acute and chronic myocarditis in the above forms of endocarditis should be kept in mind in making clinical interpretations.

Adherent Pericardium.—The myocardium in cases in which death results from adherent pericardium shows practically the same condition as is found in the myocardium in old valve defects. Most cases of adherent pericardium also have defective valves. The cause in both

TABLE II

MYOCARDIUM IN HEARTS WITH SYPHILITIC AORTITIS (106 CASES)

GROUP			CORONARY SCLEROSIS						MYOCARDIAL FIBROSIS						PROLIFERATIVE INFLAMMATION	
			SEVERE		SLIGHT		NONE		SEVERE		SLIGHT		NONE			
DEATH FROM	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Aortic insufficiency	46	43.5	1	2	8	17.5	37	80.5	–	–	9	19.5	37	80.5	3	6.5
Closure of coronary orifices	25	23.5	–	–	3	12.0	22	88.0	–	–	2	8.0	23	92.0	4	16.0
Rupture of aortic aneurysm .	35	33.0	–	–	–	–	35	100.0	–	–	–	–	35	100.0	4	11.5
Total	106		1	0.9	11	10.5	94	88.5	0	0	11	10.5	95	89.5	11	10.5

conditions is evidently a previous rheumatic infection. The degree of injury in the myocardium with an adherent pericardium, as indicated by anatomical change, is slight and evidently not the cause of the cardiac failure.

Syphilitic Aortitis.—Death from syphilitic aortitis represents about 10 per cent of all cardiac deaths. As in most other forms of valve defect, the chief change to be noted in the myocardium is hypertrophy. The myocardium was studied in 106 cases of syphilitic aortitis. Based upon the clinical course and the pathological conditions at necropsy these cases may be divided into three groups.

1. Aortic insufficiency, 46 cases (43.5 per cent).
2. Sudden death from closure of coronary orifices, 25 cases (23.5 per cent).
3. Rupture of aortic aneurysm, 35 cases (33.0 per cent).

In group I, where death results from aortic insufficiency, marked myocardial hypertrophy is noted. The condition of the coronary arteries and myocardium was studied in 46 cases of this group (Table II). Severe proximal coronary sclerosis was noted in one and slight proximal coronary sclerosis in 8. The coronary arteries showed evidence of senile sclerosis in but 9. Injury to the coronary arteries in syphilitic aortitis is unusual except at their orifices in the root of the aorta. Slight myocardial fibrosis of the atrophic type was present in 9 cases. By the atrophic type of myocardial fibrosis is meant a fraying out of the muscle fibers and a replacement with connective tissue (Fig. 3). In 37 cases (80.5 per cent) of this group no coronary sclerosis or atrophic myocardial changes were noted. In only 3 of the 46 cases (6.5 per cent) could small areas of proliferative inflammation be detected. These proliferative inflammatory areas were evidently due to syphilitic infection and were of so slight extent that it would seem they had little to do with the cardiac failure.

In Group II, where death resulted suddenly from narrowing of the coronary orifices, 25 cases were studied (Table II). Coronary sclerosis to a slight extent was found in only 3 of the 25. In the remaining 22 (88 per cent) the coronary arteries appeared normal except at their orifices in the aorta. Slight myocardial fibrosis of the atrophic type occurred in only 2 of the 25 cases. In 23 (92 per cent) there was no indication of myocardial injury following proximal coronary narrowing. In 4 (16 per cent) small areas of proliferative inflammation with lymphocytes were detected. In this group the myocardium in all but a few cases shows no anatomic change except the hypertrophy.

In Group III, or in the cases of syphilitic aortitis in which death resulted from a rupture of a syphilitic aortic aneurysm, 35 cases were studied (Table II). No coronary narrowing or myocardial fibrosis of

the atrophic type was found in any of these 35 hearts. Small areas of proliferative inflammation were found in 4 (11.5 per cent). As in the other groups the myocardium shows little anatomical change.

It seems evident that, even in a slight degree, myocarditis with syphilitic aortitis is rare and that death, except in a few cases with myocardial gummas, is seldom if ever due to a myocardial inflammatory condition or to scars resulting from inflammation.

Hypertensive Hearts.—This is the type of myocardial failure which is commonly diagnosed as due to chronic myocarditis by clinicians. On the basis of the manner in which death occurs, the 139 hypertensive hearts can be classed in four groups as follows:

1. Death with congestive failure, 78 cases (56.0 per cent).
2. Death from coronary sclerosis, 37 cases (26.5 per cent).
3. Death from cerebral hemorrhage, 16 cases (11.5 per cent).
4. Death from renal insufficiency, 8 cases (5.5 per cent).

Seventy-eight (56 per cent) of the 139 cases with hypertension are in the group having congestive heart failure (Table III). In none of these hearts is there any cellular proliferation or exudation except in those in which there are infarcts. The myocardial fibrosis bears a close relation to coronary sclerosis. There is coronary sclerosis in a severe degree in 12 (15.5 per cent) of the 78 cases, and severe myocardial fibrosis in 2 (2.5 per cent). There is slight coronary sclerosis in 54 (69 per cent) of this group and slight myocardial fibrosis in 35 (44.5 per cent). No narrowing of the coronaries is noted in 12 (15.5 per cent) and no myocardial fibrosis in 41 (52.5 per cent).

It should be observed that severe myocardial fibrosis is present in only 2.5 per cent of the group. In the remainder the fibrosis is slight or absent. It seems evident that the fibrosis is not due to inflammation and that, in a great majority of cases, the cause of the myocardial failure is some other factor than an inflammation or a fibrosis in the myocardium.

Thirty-seven (26.5 per cent) of the 139 cases with hypertension are in the group where death resulted from severe coronary sclerosis or thrombosis. Although there are many cases of death from coronary sclerosis in which there is no clinical history of a high blood pressure and in which there is no cardiac hypertrophy, only cases of coronary sclerosis with hypertension are included in this study. In hearts from cases where death occurred from coronary sclerosis without evidence of high blood pressure or cardiac hypertrophy, fibrosis is present as often and to as great an extent as in cases of coronary sclerosis with hypertension. Table III shows the involvement of the coronary arteries and the myocardium in the hypertensive cases with coronary sclerosis. Coronary thickening is present to a severe extent in all of

TABLE III

MYOCARDIUM IN HYPERTENSIVE HEARTS (139 CASES)

GROUP DEATH FROM	NO.	PER CENT	CORONARY SCLEROSIS						MYOCARDIAL FIBROSIS					
			SEVERE		SLIGHT		NONE		SEVERE		SLIGHT		NONE	
			NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Congestive failure	78	56.0	12	15.5	54	69.0	12	15.5	2	2.5	35	44.5	41	52.5
Coronary sclerosis	37	26.5	37	100.0	–	–	–	–	18	48.5	17	46.0	2	5.5
Cerebral hemorrhage	16	11.5	6	37.5	8	50.0	2	12.5	–	–	6	37.5	10	62.5
Renal insufficiency	8	5.5	1	12.5	5	62.5	2	25.0	–	–	1	12.5	7	87.5
Total	139		56	40.5	67	48.0	16	11.5	20	14.5	59	42.5	60	43.0

the 37 cases. There is thrombosis in 27 (73 per cent). While myocardial fibrosis is found in all except 2 of the 37 hearts, it is severe in only 18 (48.5 per cent). The myocardium in this group shows a greater degree of injury than is found in hearts with congestive failure. This suggests the coronary narrowing as the cause of the fibrosis. It is evident that the fibrosis of the myocardium is of slight significance as a cause of cardiac failure since in more than half of the cases the fibrosis is slight or absent.

In Table III it is seen that 16 (11.5 per cent) of the 139 cases of hyperpiesia are in the group having a mild degree of cardiac decompensation and death from cerebral hemorrhage. Severe coronary sclerosis is present in 6 (37.5 per cent). Severe myocardial fibrosis is not noted. In 8 (50 per cent) of the 16 cases there is a slight degree of coronary sclerosis and there is a slight fibrosis of the myocardium in 6 (37.5 per cent). This fibrosis appears to have resulted from the coronary narrowing but is not responsible for the death, since death was due to cerebral hemorrhage.

In Table III it is seen that only 8 (5.5 per cent) of the 139 cases are in the group with mild cardiac decompensation where death resulted from renal insufficiency. In another series of 400 cases of hyperpiesia about 10 per cent are in this group. Coronary sclerosis is present in 6 of the 8 cases but it is severe in only one. Myocardial fibrosis is found in but one case and in this the fibrosis is slight.

A summary of the involvement of the coronary arteries and the myocardium in the 139 cardiac cases with hyperpiesia is given in Table III. Coronary sclerosis is present to a severe degree in 56 (40.5 per cent). Thirty-seven of these are the cases where death occurred suddenly from coronary narrowing. Severe myocardial fibrosis is noted in only 20 (14.5 per cent) of the 139 cases. Eighteen of these 20 cases are from the group dying from coronary sclerosis. Slight coronary sclerosis is found in 67 (48 per cent) of the entire group. There is slight myocardial fibrosis in 59 (42.5 per cent). It is to be emphasized that myocardial fibrosis to a severe extent occurs in only 14.5 per cent of the 139 cases, that no fibrosis is seen in 43 per cent, and that in the remaining 42.5 per cent the fibrosis is slight and of little or no significance.

The following facts are suggested from the study of the myocardium in these 139 cases of hyperpiesia: the fibrosis found in the myocardium is not inflammatory in origin, but apparently results from a myocardial anemia following narrowing of the coronary arteries. Fibrosis of the myocardium to a severe extent is present in only about 15 per cent of the cases, most of which are in the group where death resulted from the narrowing of the coronary arteries, and even in this group less than half show myocardial fibrosis of any significance. Fibrosis of the myocardium is of little importance in bring-

ing about myocardial failure in cases of hyperpiesia. Some factor or factors not manifested anatomically have the chief part in bringing about myocardial failure in hypertensive hearts and hearts with coronary sclerosis.

Right Ventricular Hypertrophy and Dilatation.—A small group of hearts fail following hypertrophy and dilatation of the right ventricle resulting from increased pulmonary pressure. This may occur in such conditions as chronic bronchial asthma, chronic emphysema, chronic bronchiectasis, and in the so-called Ayerza's disease. Four of the 429 cases studied in this paper are in this group. Slight fibrosis is noted in all of the 4 hearts. This fibrosis appears to have resulted from an inflammatory condition since Aschoff bodies or irregular areas of proliferation are found in all. The fibrosis is present in the left ventricle while the hypertrophy is in the right ventricle. This suggests that there is no causal relationship between the increased pressure and the fibrosis. It also indicates that the slight amount of fibrosis probably has nothing to do with bringing about cardiac failure.

DISCUSSION

Two anatomical types of myocardial injury are noted in many of these 429 cases of cardiac failure. First, there are the inflammatory injuries which are shown as exudative or proliferative changes either in localized areas or scattered diffusely throughout the heart in the interstitial tissues. The inflammation shows a great tendency to be arranged about blood vessels and upon healing, to leave scars with a periarterial arrangement. The second type of myocardial injury is the myocardial fibrosis without any evidence of an association with inflammation. These scars appear as areas of atrophy of the muscle fibers with a replacement by connective tissue. This second form of myocardial scar is a definite result of coronary sclerosis of the senile type.

The inflammatory type of myocardial injury is common in all forms of rheumatic and bacterial valvular injuries, but it is rare in the myocardium in syphilitic aortitis. It occurs seldom or not at all in the myocardium in cases where death results from essential hypertension or from coronary sclerosis. The atrophic scars are rarely found in cases of cardiac failure except in the groups having hypertension and coronary sclerosis. Myocardial fibrosis of either the inflammatory or the atrophic type is seldom present to a severe extent except in the group where death results from coronary sclerosis. Here it is found in only a relatively small percentage of cases.

The result of the active myocarditis probably is somewhat of a factor in bringing about cardiac failure, but the atrophic form of fibrosis, even in its severe degree, does not seem to be of much importance as a cause of death.

It is doubtful whether the clinical diagnosis of either acute or chronic myocarditis should be made, even though such a condition commonly exists in association with a valvulitis. It is certain that what is called chronic myocarditis clinically in chronic heart failure without valvular injury is not an inflammatory condition and in most cases it is not any other condition in the myocardium showing an anatomical basis for the failure.

SUMMARY

1. Myocarditis, acute or chronic, arranged diffusely or in localized areas as Aschoff nodules or abscesses, is a common condition in the myocardium in acute and recurrent rheumatic endocarditis, in subacute bacterial endocarditis, and in old valve defects.

2. The peri-arterial scars appear to be the result of a previous bacterial infection and are frequently found in the myocardium in cases of subacute bacterial endocarditis and old valve defects.

3. Proliferative or exudative inflammation is rare in the myocardium in cases of syphilitic aortitis.

4. Scars resulting from atrophy of muscle with replacement by connective tissue following a narrowing of coronary arteries seldom occur except in the myocardium in cases of hypertension and coronary sclerosis.

5. The extent of myocardial injury as shown by anatomical changes rarely appears to be sufficient to bring about cardiac failure.

6. The conditions usually diagnosed acute or chronic myocarditis clinically cannot be demonstrated to be inflammatory processes and in most cases anatomical injuries are not seen.

7. So-called myocarditis is usually a condition of the myocardium, probably fatigue, which is not manifested anatomically.

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(*For discussion, see page* 117.)

THE RELATION OF THE ADRENALS TO THE CIRCULATORY COLLAPSE OF DIPHTHERIA*

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IN EARLIER papers from this laboratory it was shown that one of the most important factors concerned in the circulatory collapse which occurs in diphtheria is a greater or less degree of paralysis of the splanchnic nerves. This paralysis allows the abdominal vessels to relax, and these, acting as a reservoir, lessen the amount of blood to be returned to the heart and bring about a "distributive oligemia." In addition to this lack of circulating blood, there is in severe cases of diphtheria a heart profoundly affected by the toxin—a toxic parenchymatous myocarditis—and this must affect the circulation deleteriously. However, it is still an open question as to just how large a part the myocarditis plays in the circulatory failure. Indeed it has been abundantly proved that such hearts, although markedly pathological, will still maintain a satisfactory circulation provided they are supplied with sufficient blood. The vasomotor center and the muscular walls of the vessels appear to react normally. However, other structures which might be concerned in the circulatory embarrassment and which deserve careful study in this connection are the adrenal glands. Abramow,[1] one of the earlier investigators upon the reaction of the adrenals to diphtheria intoxication, described the changes produced in the glands by the toxin when it is given either in doses causing death in a comparatively short time or merely in sublethal doses. While with the small doses he believed there was evidence of stimulation of those glands, with the large doses there was evident epinephrin poverty and he ascribes the circulatory disturbance with resulting failure of the heart largely to this factor. One of the more recent writers on the subject (Harding[2]) says that in diphtheria the adrenals show a hyperchromatism with increased staining of the nuclei followed by hypochromatism progressing in places to dissolution of the nuclei and breaking down of the cells. However, it may be said that the significance of these changes is not completely understood nor the part which they may play in causing a disturbance of the function of these glands. In addition, it is not at all unlikely that some of the changes in the adrenals which have been described are not specific for diphtheria at all, as they may be present in any severe acute infection or may even be due to post-mortem processes.

The epinephrin content of the glands in diphtheria was investigated by Ehrmann,[3] who used the isolated frog's eye method of assay.

*From The Pharmacological Laboratory of the University of Michigan.
Presented at the meeting of the Association of American Physicians, Atlantic City, N. J., May 1927.

He reported that even in severe cases of diphtheria intoxication with marked pathological changes in the glands there was still epinephrin present in the blood and that it might even be present in an increased amount. It must be pointed out, however, that the method of assay utilized by Ehrmann has not been found to be satisfactory by many of the other workers and therefore his conclusions cannot be accepted at their face value. Elliott[4] in the same year reported that the staining properties of the cells of the adrenals when treated with mixtures containing chromic acid were much diminished after poisoning with the toxin and that the intensity of the stain corresponded with the amount of epinephrin which could be extracted from the gland. In a later paper[5] he states that the amount of epinephrin was much diminished in the adrenals of cats which had died of diphtheria and that the amount was decreased to a greater extent on the side with intact splanchnics as compared with the side on which the nerve had been cut. For instance, with an average yield of 0.25 mg. of epinephrin from a normal gland he obtained from the adrenal of a diphtheritic animal on the side with the intact nerve only 0.02 mg. while on the side with the nerve cut he found amounts varying from 0.15 mg. to 0.22 mg. The difference between the two sides was very striking in every case. Elliott concluded that the action of the *toxin* was *not* a direct one upon the gland but was due to some action which reached the glands by way of the splanchnics. He did not think that the exhaustion of the epinephrin was a primary cause of death. Ritchie and Bruce[6] found, much like Abramow, that in the more acute type of diphtheria in guinea pigs there was a considerable diminution in epinephrin while in more protracted cases there was complete exhaustion. So also Broberg[7] reported changes in the adrenals in protracted diphtheria but stated that they were no more than could be explained by the general cachexia. Lucksch[8] has also called attention to the fact that in this intoxication the epinephrin may be partly or wholly lost. The adrenals of some guinea pigs used by him were entirely inactive in so far as epinephrin was concerned, and in a dog which died after four days' illness he found no epinephrin. Also in children dead of diphtheria he found a diminished epinephrin content and he believes that such a change may be important in determining the course of the illness of the individual. More recently Hartman and Macdonald[9] reported that they were unable to demonstrate any increase in epinephrin in the blood of cats following the injection of diphtheria toxin. An examination of the glands by staining methods showed that at times the medulla appeared to be depleted but usually epinephrin was present in patches or in limited groups of cells. Finally Molinelli[10] has shown that in dogs and rats which have been injected with diphtheria toxin the weight of the adrenals is not increased. They may possess a normal aspect or may appear congested, but the amount of

epinephrin contained is in general diminished. He says also that the amount of epinephrin in the blood obtained from the suprarenal vein is also markedly lessened.

It will be seen by these brief references to the literature that most workers find a lessened amount of epinephrin in the adrenals of diphtheritic animals but it will also be noted that most of the reports are based upon impressions gained by a study of the intensity of staining reactions rather than upon definite estimations of the amount of the alkaloid which could be extracted from the glands. Accordingly, in connection with our studies upon the causes of the circulatory collapse in diphtheria, we have also investigated the epinephrin content of the adrenals in an effort to shed further light upon the question.

In the first place it was necessary to establish a normal epinephrin content for dogs as most of the figures which are available in the literature were obtained from animals which had been used in laboratory experimental work and which, therefore, had been subjected to various operative procedures in addition to a more or less prolonged anesthesia. Accordingly, we secured our normal controls from dogs immediately after anesthesia was complete, the anesthetic consisting of a subcutaneous injection of morphine (75 mg.) followed by urethane (1.5 gr. per kg.) given by means of a stomach tube. These same animals from which the adrenals had been removed were then used for the assay of both the normal and the diphtheritic glands; in many cases, therefore, the assay of the normal glands was carried out upon the same animal from which they had been removed.

We secured the diphtheritic glands from dogs immediately after death from the effects of the toxin. The epinephrin was extracted and then by means of the blood pressure method the amount of epinephrin in the solution was assayed by comparing it with a standard solution of epinephrin (Metz). The method of extracting the epinephrin from the glands was as follows, and was essentially that described by Folin, Cannon and Denis.[11]

After the glands had been removed from either the normal animal or from the animal dead from diphtheria, they were carefully separated from the surrounding fat and connective tissue, weighed, cut into small pieces and then ground in an agate mortar with N/10 hydrochloric acid. The mixture was placed in an Erlenmeyer flask and enough of the acid added to make 7.5 c.c. for each gram of gland. Three times as much water was then added and the mixture boiled. To this was added 10 per cent sodium acetate, 5 c.c. for each 15 c.c. of HCl, and the mixture brought to the boiling point again. It was then filtered and transferred to a volumetric flask (50 c.c. for each gram of gland) and filled to the mark. The standard solution was prepared from the Metz synthetic epinephrin by adding sufficient N/10 HCl to the alkaloid in water to bring it into solution and then diluting it with water to the desired strength, 1:1000. This solution was further diluted for use. The technic of the biological assay is well known. The dog being fully anesthetized, cannulas are inserted in the trachea for artificial respiration, in the carotid for the blood pressure record, and in the femoral veins for

the injection of the solutions. The vagi are cut and artificial respiration instituted. The two solutions—the standard and the unknown—are now injected in appropriate doses until a suitable comparison of strengths is found from which the epinephrin content of the unknown solution can be calculated.

The results obtained from the normal dogs are as follows:

Dog	*Weight*	*Weight of adrenals in milligrams*	*Total epinephrin in milligrams*	*Epinephrin per gram of gland*
1	11 Kg.	1250	1.74	1.39
2	6 Kg.	1025	1.10	1.07
3	9 Kg.	1100	1.15	1.05

These figures show in general a reasonable agreement with the figures usually given for the amount of epinephrin in the glands of the normal dog, viz., 0.1 per cent of the moist weight.

In considering the results obtained from the diphtheritic dogs, it is important to have information concerning the history of the disease in the individual animal in order that a proper comparison may be made with the conditions as found in the human subject. The dose of toxin must not be too large or the course of the disease will be so brief as to make a comparison impossible. Accordingly a history in briefest terms of each animal is given herewith.

Dog 1 D Weight 10 Kg.
12/2/26 Toxin 0.002 c.c. subcutaneously.
12/4/26 Toxin 0.002 c.c. subcutaneously.
12/6/26 Toxin 0.0015 c.c. subcutaneously.
12/7/26 Dog quiet—not eating.
12/8/26
9 A.M. Deeply apathetic—bloody vomitus and movements.
10 A.M. Stopped breathing. Artificial respiration, 10 per cent glucose intravenously.
Duration of intoxication—6 days.

Dog 2 D Weight 9 Kg.
2/21/27 Toxin 0.007 c.c. subcutaneously.
2/23/27 Very quiet, apathetic.
2/24/27 Toxin 0.01 c.c. Dog apathetic.
2/25/27 Dying, operated. Duration of intoxication—4 days.

Dog 3 D Weight 9.5 Kg.
2/21/27 Toxin 0.005 c.c. subcutaneously.
2/24/27 Toxin 0.003 c.c. subcutaneously.
2/25/27 Toxin 0.008 c.c. subcutaneously.
3/ 2/27 Quiet. Toxin 0.002 c.c. subcutaneously.
3/ 3/27 Dying. Operated.
Duration of intoxication—10 days.

Dog 4 D Weight 13.5 Kg.
2/28/27 Toxin 0.01 c.c. subcutaneously.
3/ 1/27 Inactive.
3/ 2/27 Toxin 0.01 c.c. subcutaneously.
3/ 5/27 Toxin 0.01 c.c. subcutaneously.
3/ 7/27 Dying. 3 P.M. operated.
Duration of intoxication—7 days.

The estimation of the epinephrin in the diphtheritic dogs, histories of which are given above, is as follows:

Dog	Weight	Weight of adrenals in milligrams	Epinephrin in milligrams	Epinephrin per gram of gland
1 D	10.0	1840	0.30	0.16
2 D	9.0	1800	1.25	0.69
3 D	9.5	1450	1.05	0.73
4 D	13.5	1725	1.05	0.61

These figures giving the epinephrin content of the adrenals in animals dying of diphtheria confirm the findings of Lucksch, Elliott and the others who report a lowering in epinephrin content in the glands in this disease, but what importance this diminution has in the life of the animal is not so easy to answer. In the first place the action probably is not specific for diphtheria. Lucksch, in particular, has shown that in many diseases, especially in tuberculosis, the epinephrin content of the glands may be lowered. It is not unlikely that Broberg is right when he says that the change may be explained by the general cachexia. It is certainly true that the factor of cachexia may play a rôle in the results obtained in the animals. Our dogs all showed symptoms of an acute illness, being very quiet on the day following the injection, eating and drinking little or nothing, and finally toward the end being apathetic and in some cases comatose. On the other hand, it would certainly seem probable that a diminution of epinephrin in the glands to perhaps 20 per cent of the normal amount or even as reported by some workers to a total absence of the alkaloid, could not help but be of importance in the expectancy of life of the individual. However, it is probably not a sudden exhaustion of the epinephrin which takes place. All the evidence is that it is a gradual affair extending over days while the typical circulatory collapse in diphtheria is an acute phenomenon—a matter of an hour or two—making it appear most likely that the adrenal exhaustion is not an important factor in the collapse but is merely an associated phenomenon.

SUMMARY

In diphtheria there is a marked diminution in the amount of epinephrin in the adrenal glands. This decrease in epinephrin is probably not the cause of the circulatory collapse.

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PAROXYSMAL VENTRICULAR TACHYCARDIA WITH ALTERNATING COMPLEXES DUE TO DIGITALIS INTOXICATION*

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IN THE past few years a considerable number of examples of paroxysmal ventricular tachycardia have been reported[1, 2, 3] and several authors have commented upon the probable relationship of the tachycardia to the administration of digitalis; Reid[4] particularly has emphasized the close association between the abnormal mechanism and preceding large doses of the drug. That the relationship is not an invariable one is clear, for in many of the recorded cases digitalis had not been given during the preceding days or weeks.[3] In 1922, Schwensen[5] published an extraordinary electrocardiogram displaying regular alternation of upward and downward ventricular deflections at a rate of 180 per minute; it was obtained from a patient whose electrocardiograms before and after the unusual mechanism showed auricular fibrillation. This was the first published example of the alternating type of ventricular tachycardia in the human being; similar curves were recorded in 1923 by Felberbaum,[6] in 1924 by Reid,[4] and two in 1925 by Luten.[7] In all five cases auricular fibrillation had been present before the development of the unusual ventricular tachycardia, and in three of them it was present after the tachycardia ceased; all of the patients had received digitalis in large doses, and the unusual mechanism was regarded in each instance as probably due to the administration of that drug. Reid's case differs from the others in one important respect, in that the alternation in direction of the ventricular complexes was present for only a few cycles about thirty seconds before the death of the patient, and immediately preceded the onset of ventricular fibrillation.

In each of the four reports mentioned above, the origin of the tachycardia is briefly discussed, each author recognizing that there are two possible explanations of the unusual rhythm. One is that there is a single focus, situated probably in the A-V node or in the A-V bundle above its bifurcation, sending out rhythmic impulses which travel alternately along the right and left branches of the bundle. This explanation assumes that the branch which has just transmitted an impulse is partially or wholly refractory to the next succeeding one; it is further assumed (Luten) that digitalis may be responsible for such an interference with bundle-branch conduction.

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The alternative explanation is that there are two foci sending out impulses, one in either ventricle, and that the tachycardia is composed of a rapid succession of ectopic beats arising alternately in right and left ventricles. In none of the reported cases has it been possible definitely to decide which type of mechanism was responsible.

The following five cases are reported partly because they represent a considerable addition to the small number of similar cases now on record, but chiefly because the electrocardiograms from several of them appear to throw light upon the nature of the mechanism involved, and because they provide additional evidence tending to show that digitalis is responsible for the condition. The present communication is concerned *only* with those instances of paroxysmal tachycardia in which there is constant alternation of upward and downward ventricular complexes at a rate usually exceeding 150 per minute. The essential facts of the histories will be presented briefly, and the important features of the electrocardiograms discussed subsequently.

CLINICAL REPORTS

CASE 1.—An Irish teamster, fifty-nine years of age, entered the hospital on January 23, complaining of shortness of breath, cough, and swelling of the legs. He stated that dyspnea had first become troublesome about four or five weeks previously and that orthopnea and swelling of the feet had been noted several days later. All symptoms increased rapidly; swelling of arms and hands was first observed two days before he came to the hospital. The previous history was irrelevant.

Physical examination at the time of admission showed orthopnea, urgent dyspnea, deep purplish cyanosis of lips, ears, and nail-beds of fingers, conspicuous engorgement of the neck veins, and well-marked nodding of the head. There was frequent unproductive cough. There were signs of fluid in both pleural cavities below the angles of the scapulae. The heart was considerably enlarged, the apex impulse being in the sixth left intercostal space in the anterior axillary line; the right margin of percussion dullness in the fourth right intercostal space was 4 *cm.* to the right of the median line. The auscultatory signs were those of stenosis and insufficiency of the mitral and aortic valves. The rhythm was regular, the rate 136 per minute. The liver edge was felt 8 cm. below the costal border in the right mammillary line; the tip of the spleen was just palpable. There was great edema of the subcutaneous tissues from the level of the umbilicus downward. The peripheral arteries were hard and tortuous. The blood pressure ranged from 115 to 130 mm. Hg. systolic, and 88 to 100 mm. diastolic.

The Wassermann reaction on the blood serum was negative. A seven-foot x-ray film of the heart showed considerable enlargement. Other laboratory data were not of importance.

Course and Treatment.—The patient was admitted at noon on Jan. 23. His weight was 133 pounds. Digitalis in the form of the powdered leaf was administered as follows: 0.6 gm. at 1 P.M., 0.4 gm. at 4 P.M., and 0.4 gm. at 8 P.M. on the twenty-third; 0.2 gm. at 8 A.M. and at noon on the twenty-fourth; a total of 1.8 gm. in twenty-four hours. On the morning of the twenty-fourth, a pleural friction rub was detected in the right axilla; several hours later the heart rate was found to be 160 per minute and apparently regular. An electrocardiogram

was taken and revealed the mechanism illustrated in Fig. 1. The tachycardia continued without interruption, so far as is known, throughout the remainder of the day and the night. On the following day (Jan. 25) there were clear signs of pulmonary infarction, but no fever. Throughout the day there were paroxysms of tachycardia, lasting from several minutes to several hours; the rate during these periods was usually very near 150 per minute, while between the paroxysms the rate was approximately 100 per minute. Electrocardiograms showed that the tachycardia was always of the same type, but there were minor variations in the size of the ventricular deflections during different paroxysms (Fig. 2). On the twenty-sixth, paroxysms of tachycardia were infrequent, but the pulmonary condition had extended and the patient seemed worse. During the next two days no paroxysms of tachycardia were detected by auscultation or in electrocardiograms, but the temperature rose steadily, the respirations increased in rate, signs of bronchopneumonia became widespread, and the patient died at noon on Jan. 28.

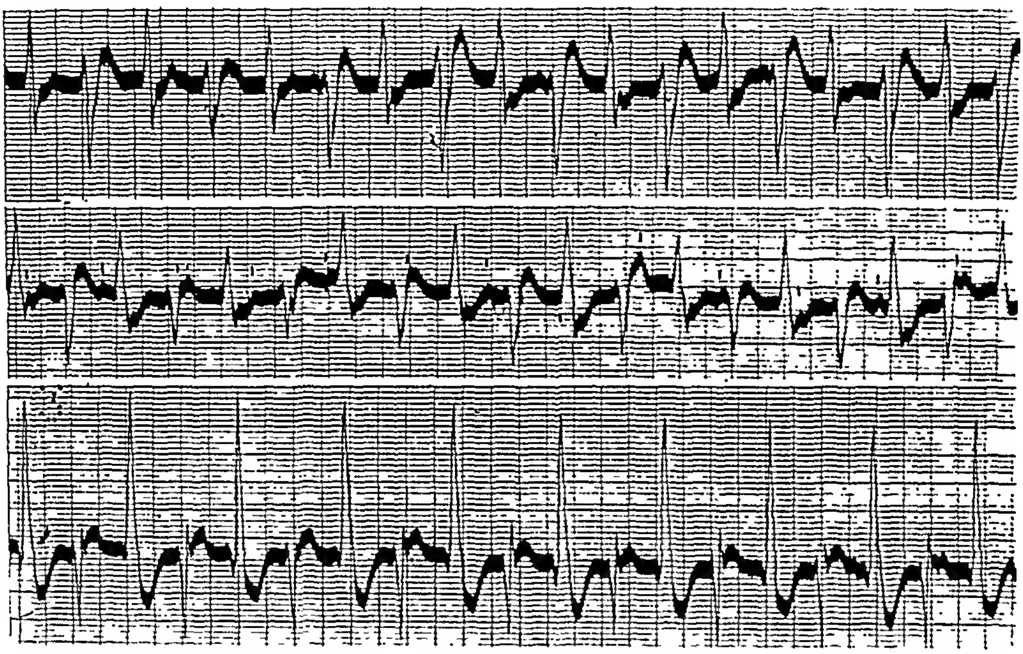

Fig. 1.—Case 1. Leads I, II, and III. Record obtained on Jan. 24. The auricular rate is 102.85 and the ventricular rate 146.9 per minute. The ventricular rhythm is slightly but definitely irregular in all leads. In Lead II, auricular waves are marked by small vertical lines. Notice the minor variations in form of ventricular deflections. (In this and all subsequent electrocardiograms distances between abscissae represent 10^{-4} volts, and time is in fifths of a second. Figures are full size except when otherwise stated. In many instances the stated rate has been calculated from long strips of film rather than from the published figure.) (x ⅔)

Autopsy.—There were signs of general passive congestion; there was free fluid in the pleural cavities and in the peritoneal cavity, and edema of the subcutaneous tissues. The lungs showed multiple areas of infarction. The liver extended 6 cm. below the costal border. The heart was greatly enlarged; it weighed 850 gm. There was an area of fresh fibrinous pericarditis near the apex of the left ventricle, about 4 cm. in diameter. The ventricular cavities were very large, especially the left. The wall of the right ventricle averaged 5 mm. in thickness, that of the left, 18 mm. There was a mural thrombus in the right auricular appendage. On the inner surface of the left ventricle near its apex, the location corresponding to the area of pericarditis, there was a thrombus firmly adherent to the wall, and undergoing organization. On section it was found to be hollow, the center having become necrotic. The ventricular wall beneath the thrombus was approximately

one-third the thickness of the wall elsewhere; its outer half was composed of dense fibrous tissue and its inner half of dull, lusterless, necrotic-looking muscle. A thrombus quite similar in appearance, but apparently more recent, was attached to the interventricular septum at the apex of the right ventricle. The tricuspid and pulmonary valves were normal in appearance. The mitral orifice was narrowed; the valve leaflets were thickened along the line of closure and showed many small irregular vegetations. The papillary muscles were greatly thickened and slightly flattened. The aortic valve cusps were thickened, sclerotic and adherent, with extreme calcification. The valve opening was reduced to a mere slit. The orifices

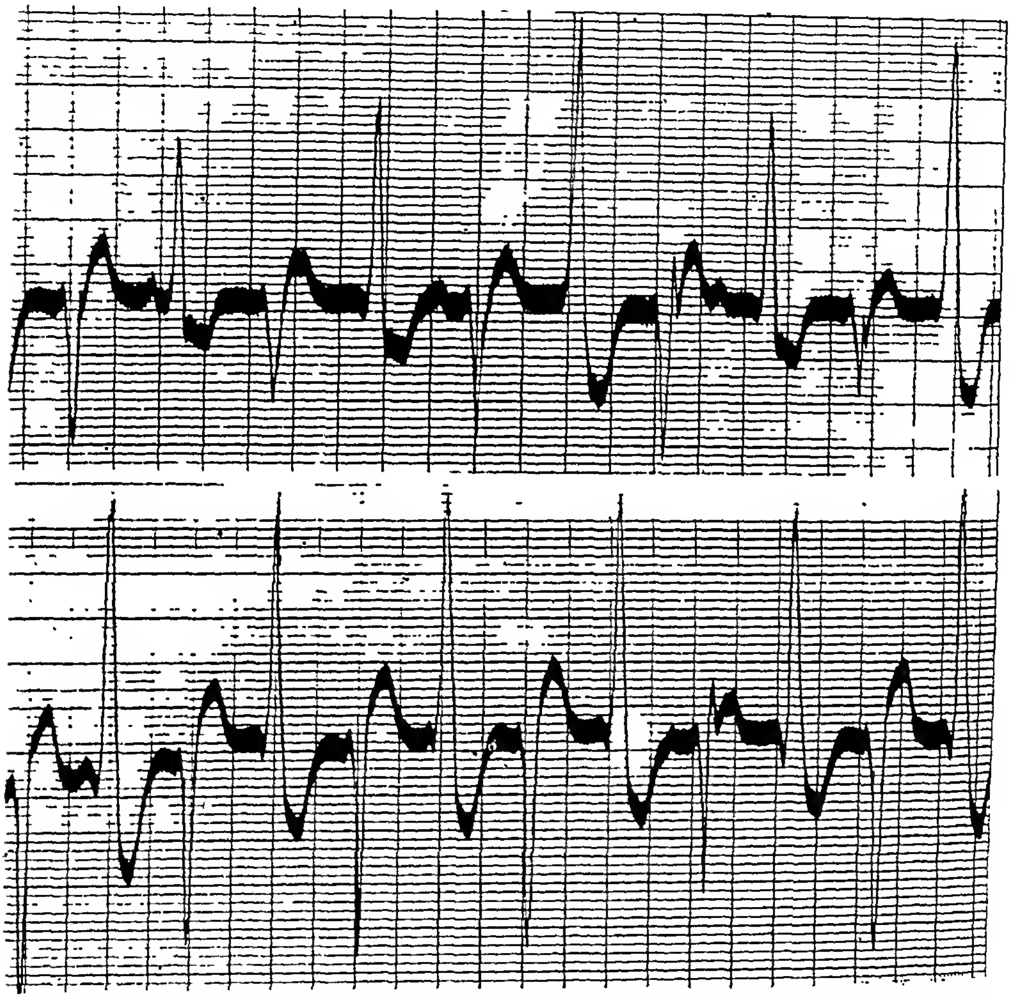

Fig. 2.—Case 1. Upper curve, Lead III, Jan. 24. Auricular rate, 93.7, ventricular rate, 138.46 per minute. Lower curve, Lead III, Jan. 25. Auricular rate not determined, ventricular rate 145.4 per minute. Notice especially the *differences in size and shape of ventricular complexes.*

of the coronary arteries were patent, and no closure of a vessel could be demonstrated by dissection or by stereoscopic roentgenograms taken after injection of the coronary vessels with barium gelatine.

Microscopic examination of sections from the heart showed an extreme degree of hypertrophy of the muscle fibers, with widespread fibrosis, especially about the blood vessels. A section through the thrombus in the left ventricle showed the picture of organization, with many fibroblasts and small capillaries; in places, endothelium could be seen growing over the surface of the thrombus. There was necrosis of the muscle fibers beneath the thrombus, with fibrosis in the outer

portion of the ventricular wall. Microscopic study of the vegetations on the mitral valve revealed them as dense, acellular connective tissue.

The anatomical diagnosis was: healed mitral endocarditis, healed and calcified aortic endocarditis with advanced stenosis, diffuse fibrosis of myocardium, organizing mural thrombi in ventricles, organizing pericarditis, cardiac hypertrophy and dilatation, chronic passive congestion of the viscera with general anasarca, pulmonary infarcts.

Electrocardiograms: Electrocardiograms were obtained at frequent intervals during the four days beginning with Jan. 24; several of them are reproduced in Figs. 1 to 4. Fig. 1 is taken from the first record secured on Jan. 24; it shows the type of tachycardia, with regular alternation in the direction of the ventricular complexes, which forms the subject of this paper. Numerous curves depicting this type of mechanism were secured during this and the two following days; some of

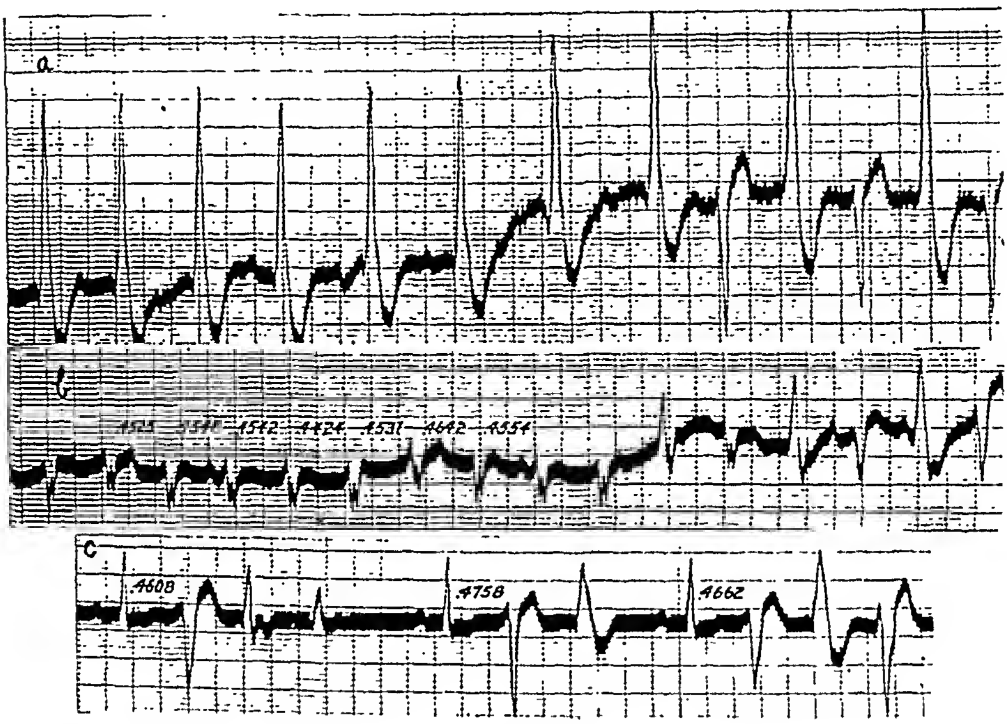

Fig. 3.—Case 1. *a*, Lead III, Jan. 25; *b*, Lead II, Jan. 24. These show the change from a tachycardia composed of precisely similar complexes to one in which there is regular alternation in direction of successive deflections. Auricular waves are distinct throughout *b*. *c*, Lead I, Jan. 26. Three normal beats, each followed after a similar interval by a group of ectopic ventricular beats, the last of which is probably the beginning of a paroxysm. Auricular waves are distinct and regular. (x ⅔)

them were precisely like those of Fig. 1, and several showed slight differences in the size or configuration of the ventricular deflections, especially in Lead III. In the first two leads of Fig. 1 many auricular waves can be identified with certainty; these, as well as the position of those which are buried in the ventricular complexes, have been marked in Lead II, by placing opposite each of them a small vertical line. It is found that the auricular rhythm is perfectly regular and the rate 102.85 per minute, while the ventricular rate, measured over the same portion of film, is 146.9 per minute. Auricular waves are present in only two places in Lead III, toward the end.

Fig. 2, containing two portions of Lead III from electrocardiograms taken on different days, illustrates the minor variations in size and form of the ventricular complexes already mentioned. The upper curve of this figure was inserted because

it represents the lowest rate observed in any records from this patient, and also displays auricular waves more clearly than any other similar lead. The rate of the auricles is 93.7, that of the ventricles 136.46, per minute.

Fig. 3, *a* is a portion of Lead III from a record secured on Jan. 25; *b* is a portion of Lead II from a record obtained on Jan. 24, and *c* is a strip of Lead I from one of the curves of Jan. 26. The change from an undirectional paroxysm to one in which there is alternation in direction of the ventricular deflections is clearly shown in *a* and *b*. The latter portion of the curve in *a* is so distorted by extrinsic current as to permit no statement about the presence of auricular waves, but such waves can be clearly seen in *b*, occurring regularly and at a rate distinctly slower than that of the ventricles. In *c* there are shown three normal ventricular complexes, each preceded at a normal interval by an auricular summit. Each of the first two complexes is followed by a group of ectopic ventricular beats; the third is followed by three such beats which presumably represent the beginning of

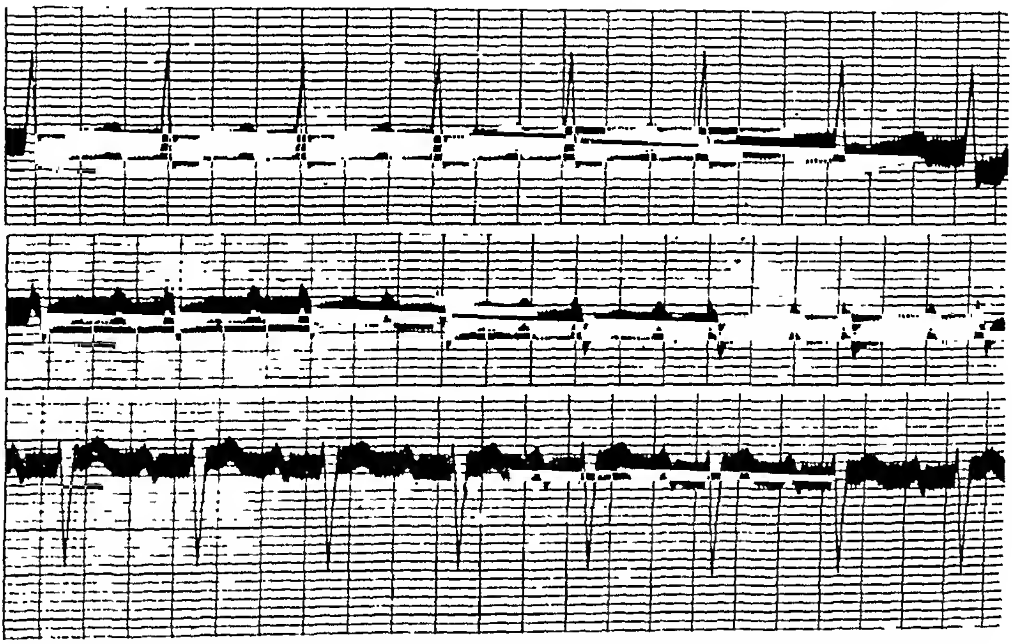

Fig. 4.—Case 1. Three usual leads; I and II taken on Jan. 25, III on Jan. 26. The A-V conduction time is prolonged in all leads, but more in the curve of Jan. 25. Notice especially the direction of the ventricular complexes in Leads I and III.

a paroxysm, although this cannot be asserted with great confidence. The intervals separating the normal beats from the ectopic beats that follow are of almost identical length.

Fig. 4 represents the normal type of ventricular complexes for this patient. Leads I and II are from a record taken on Jan. 25; Lead III from one taken on the following day. The A-V conduction interval is prolonged in all leads, but less in Lead III than in Leads I and II; the interval is steadily approaching normal.

Comment.—The course of events in this patient seems clear. A man with advaced congestive heart failure and normal cardiac mechanism received an amount of digitalis considerably greater than that necessary for complete therapeutic effects, as gauged by his body weight. Just before the last fractional dose was given, it was found that the

normal cardiac mechanism had changed to one in which the ventricles were beating much more rapidly than the auricles, and electrocardiograms showed constant alternation in the direction of the ventricular deflections. This abnormal mechanism prevailed, so far as could be ascertained by frequent observation, for about twenty hours before the normal mechanism was restored. When the normal sequence of chamber contraction was resumed, the A-V conduction time was prolonged; partial heart-block was present. During this day (Jan. 25) paroxysms similar in nature to the original one, but of relatively brief duration, occurred many times; on the following day they occurred less frequently and were of shorter duration. The A-V conduction time, although still prolonged beyond the normal, was shorter than on the preceding day. The regular rhythm between the paroxysms was frequently interrupted by ectopic ventricular beats, occurring singly or in groups of two or three. On Jan. 27 neither paroxysms of tachycardia nor ectopic ventricular beats were detected, but the P-R interval was still slightly more than 0.2 second. On the morning of the twenty-eighth, four hours before the patient's death, the electrocardiogram showed normal mechanism.

Apart from the nature of the mechanism responsible for the curious alternating ventricular tachycardia, the point of chief interest and importance is the steady decrease in the length and frequency of the paroxysms of tachycardia until they were replaced by ectopic beats, which themselves became rapidly less frequent and disappeared completely. Coincident with this change in the abnormal mechanism, there was a similar change in the length of A-V conduction time; considerably prolonged at first, it became constantly shorter and, after three days, was within normal limits. There was thus a perfect, orderly transition from abnormal to normal through a series of defined stages each of which represented a less advanced disturbance than the preceding one. If the progression had been from normal to abnormal, each day revealing a disturbance of higher grade, there would probably be little hesitation in accepting it as evidence of increasing digitalis effects upon the heart. There is equally good reason for believing that the events as pictured represent steadily decreasing digitalis effects, coincident with the excretion of the drug from the body.

Case 2.—A negro woman, fifty-three years of age, was admitted to the hospital on March 25 because of difficulty in breathing and swelling of the extremities. Eleven months earlier she had been troubled by headaches, dizziness, and blurring of vision, and at that time she was found to have hypertension. Four months before entry, she was said to have had severe "cardiac asthma"; one month later she entered a hospital because of increasing dyspnea and edema. Her subsequent history was one of steadily increasing congestive heart failure. The past history was irrelevant.

Examination revealed orthopnea, dyspnea, and moderate cyanosis of the mucous membranes. There was but slight fullness of the neck veins. The heart was considerably enlarged, the rhythm regular, the rate 120 per minute. There was a systolic murmur over the lower precordium. Signs of congestion were present over the bases of the lungs, the edge of the liver was 10 cm. below the costal margin in the right midclavicular line, and there was evidence of a moderate amount of free fluid in the abdomen. There was great edema of the subcutaneous tissues below the level of the umbilicus. There was moderate thickening of the peripheral arteries; the blood pressure was 160 mm. Hg. systolic, 100 mm. diastolic; subsequently it varied between 125 and 160 mm. systolic, 90 and 100 mm. diastolic. The blood Wassermann reaction was negative.

Course and Treatment.—The patient's weight was 161 pounds; later, when edema was no longer present, it was 133 pounds. She received no digitalis for two days. On March 27, she received 1.1 gm. of the powdered leaf; on March 28,

Fig. 5.—Case 2. Three usual leads; left bundle-branch block. Numerous curves of precisely similar form were obtained before and after the periods of tachycardia. Duration of ventricular complexes is indicated in Lead I.

0.4 gm.; on the morning of March 29, 0.2 gm. Several hours after this last dose, the heart rate was found to be much more rapid; an electrocardiogram was taken and revealed the alternating type of mechanism reproduced in Fig. 6. Paroxysms of tachycardia of this type occurred with decreasing frequency for three days, and then ceased. Electrocardiograms showed a return of sinus rhythm, with left bundle-branch block (Fig. 5). Digitalis was resumed on April 1; 0.2 gm. was given on April 1 and 2, 0.4 gm. on the fourth, and 0.2 gm. on the fifth. On the morning of the seventh, paroxysmal tachycardia was again present, and it occurred frequently for three days. Electrocardiograms showed the same type of alternating mechanism as that observed during the earlier days of the disorder. By April 11 the usual cardiac mechanism had been resumed, and neither paroxysms of tachycardia nor ectopic beats were detected during the remainder of her life. She died two weeks later, apparently as the result of pulmonary infection subsequent to infarction of the lung.

Autopsy.—There was very slight edema of the ankles. The right pleural cavity contained a small amount of free fluid. The heart was much enlarged, weighing 695 gm. after injection of the coronary arterial system with barium gelatine. The left ventricular cavity was large and its wall greatly hypertrophied, measuring 18 mm. in thickness. In the ventricle were numerous small ball thrombi, attached to the wall by thin pedicles. All valves appeared normal. The myocardium showed no fibrosis on macroscopic examination, and the coronary arteries were patent.

Microscopic examination of sections from the ventricles revealed great hypertrophy of the muscle fibers. Striations were quite distinct. There was slight dif-

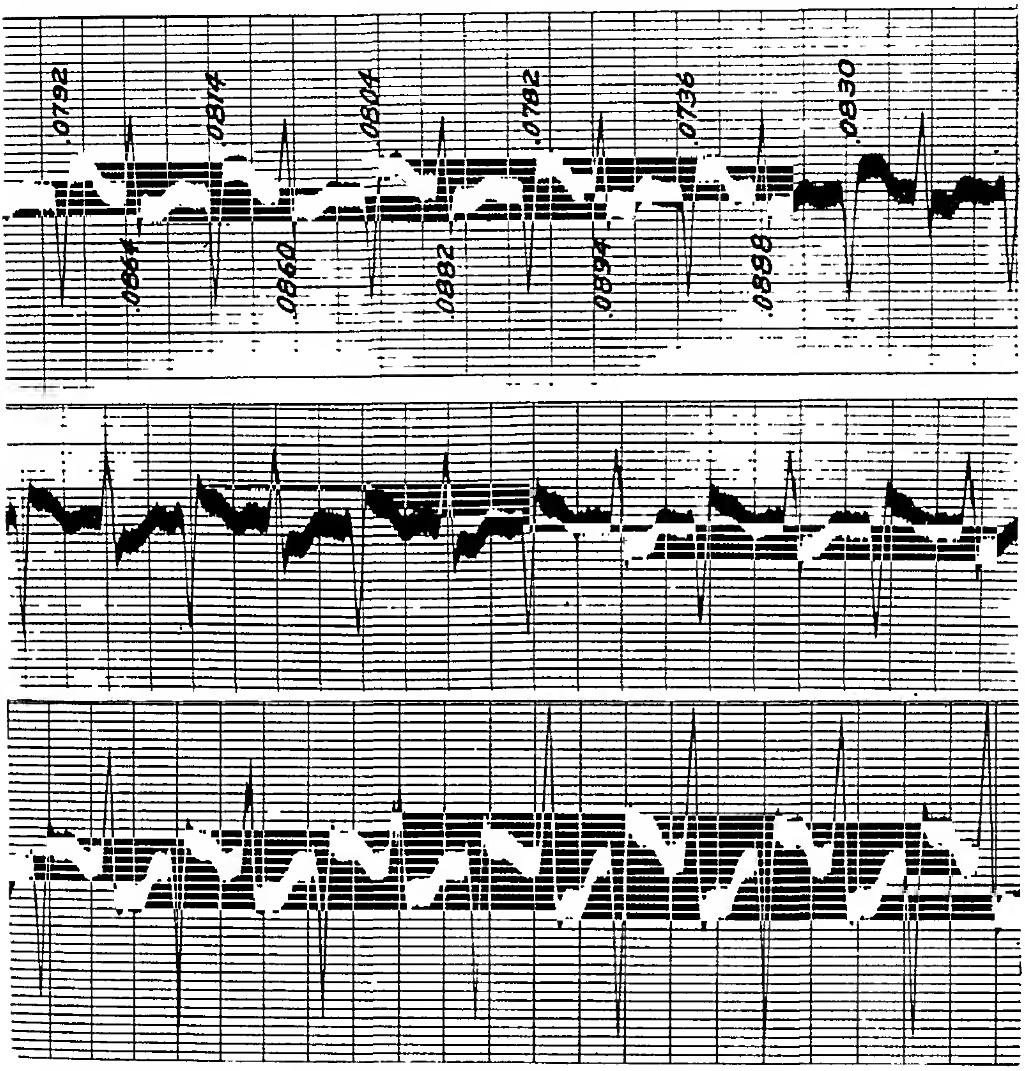

Fig. 6.—Case 2. Three usual leads, taken on April 8. Auricular waves not identified with certainty; ventricular rate varies from 163 to 180 per minute. Notice that the total duration of the ventricular deflections is less than in the preceding figure.

fuse increase in fibrous tissue. The small branches of the coronary arteries appeared normal, but in some of the larger branches there were sclerotic plaques and small accumulations of lymphocytic cells in and about the vessel wall.

Unfortunately, the examination of the conduction system could not be made as complete as desired, because the blocks of tissue removed for study did not include the bifurcation of the A-V bundle into its two main stems. Serial sections of a large portion of the interventricular septum were prepared; branches of the right and left divisions of the A-V bundle were identified readily, and presented

an extraordinary contrast in appearance. The tissue composing the right bundle-branch and its ramifications appeared entirely normal. The cytoplasm of the cells forming the left branch of the conduction system was vacuolated, extremely granular, and stained poorly. The cells appeared swollen; many contained no nuclei, while others contained only shadows of nuclei or pyknotic nuclear fragments. There was no cellular reaction of any sort surrounding the bundle-branch and its ramifications or infiltrating the adjacent myocardium. The general appearance suggested that the change was a degenerative rather than an inflammatory one, but the mechanism causing the lesion was not revealed in any of the sections.

Electrocardiograms.—Electrocardiograms were obtained at frequent intervals from the day of this patient's admission to the hospital until her death one month later. With a single exception, they were of two types only; they revealed the widened notched complexes typical of left bundle-branch block, with normal A-V conduction, or they showed paroxysmal tachycardia of the alternating type. Typical specimens of the two mechanisms are reproduced in Figs. 5 and 6, and the total duration of the ventricular deflections is indicated in corresponding leads.* Fig. 6 was selected from a number of similar records because the change in the form of the ventricular complexes in Lead III is greater than in any other electrocardiogram obtained. The only curve not conforming to the two types just

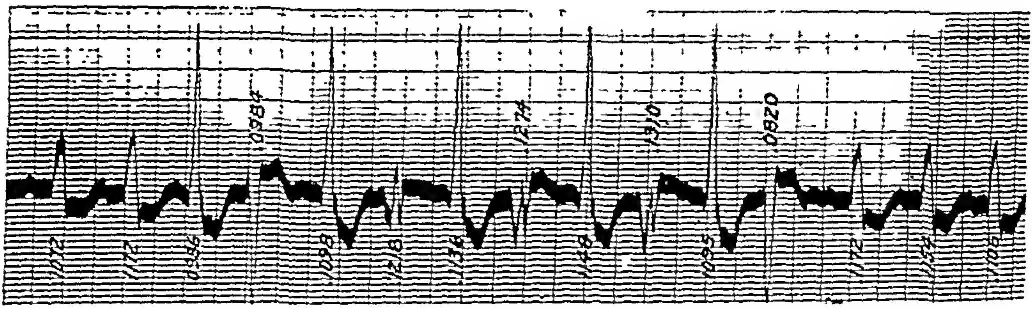

Fig. 7.—Case 2. Lead III, taken April 1. There are notable differences in the form and duration of the ventricular complexes during the short paroxysm. Auricular waves may be discerned in places through the paroxysm; their rate is 123.5 per minute, while that of the ventricles in 141.1. (x 2/3)

mentioned is shown in Fig. 7, which is from Lead III of a record taken April 1. It contains a complete short paroxysm of tachycardia in which the upward ventricular deflections are all alike, while the downward ones are of two distinct forms. The rate of auricles and ventricles during the preceding normal mechanism is 123.5 per minute; the auricular rate remains unaltered through the paroxysm, while that of the ventricles rises to 141.1 per minute. The typical bundle-branch block complexes are present immediately upon the conclusion of the paroxysm; there are no transitional forms.

Comment.—In considering the probable relationship between the administration of digitalis and alternating ventricular tachycardia, the case just presented is of peculiar importance, and seems to indicate fairly clearly that the relation was that of cause and effect. Tachycardia first appeared during the course of digitalis therapy, after 1.7 gm. had been given, and ceased gradually when the drug was discontinued; the abnormal rhythm reappeared when digitalis was again administered, and ceased when digitalis was stopped. The other

*All intervals marked upon the figures were measured by means of a comparator.

medication employed in this patient cannot reasonably be suspected of having caused the tachycardia; luminal and codeine sulphate were used freely during the first two days after her admission, novasurol was given once on April 4, three days after the first series of paroxysms occurred and three days before the second, and a single dose of theocin was given on the day of the first paroxysm. The last two drugs were administered later, in larger doses, without any effect upon the cardiac mechanism.

The electrocardiographic curves appear to be of the utmost significance in elucidating the nature of the mechanism responsible for the alternating tachycardia; this aspect of the matter will be fully discussed in the latter portion of the paper. So far as is known, this is the first recorded example of this type of tachycardia in a patient with preexisting bundle-branch block.

CASE 3.—A woman, forty-two years of age, entered the hospital on August 22 for the relief of symptoms of advanced congestive heart failure. Dyspnea and orthopnea had been noted about a year previously; edema of the lower extremities appeared shortly afterward. Symptoms became less following great restriction of physical activity. Four months before her admission, she contracted a severe respiratory tract infection, with fever, cough, and expectoration; shortly after the beginning of this infection, dyspnea and orthopnea reappeared and edema increased. All symptoms became gradually more severe from that time until she came to the hospital. The past history contained no facts of apparent significance.

The patient looked sick. There was orthopnea and slight cyanosis. Respirations were hurried and shallow, but not labored. There was no engorgement of the neck veins when she sat upright. The heart was moderately enlarged, the rhythm fundamentally regular, with occasional premature beats; the rate was 130 per minute. The heart sounds were clear and of normal intensity; a soft systolic murmur was audible over most of the precordium. The lungs showed persistent crackling râles over the lower lobes; the liver edge was felt 5 cm. below the costal margin in the right midclavicular line, and was tender. There was considerable edema of the subcutaneous tissues of the lower abdomen, the lower back, and the lower extremities. The radial arteries were slightly thickened; the retinal arteries showed moderate sclerosis. The blood pressure was 170 mm. Hg. systolic, 130 mm. diastolic. The urine constantly showed a very faint trace of albumin, with epithelial cells and leucocytes and occasional hyaline and granular casts. The excretion of phenolsulphonephthalein in two hours and ten minutes after the intramuscular injection of 1 c.c. was 40 per cent; the nonprotein nitrogen of the blood was 35 mg. per 100 c.c. Examinations of the blood revealed nothing abnormal. The blood Wassermann reaction was negative. The clinical diagnosis was arteriosclerosis with hypertension and heart disease; congestive heart failure.

Course and Treatment.—The patient was admitted late in the afternoon of August 22. Her weight was estimated at 135 pounds without edema. She stated that she had not received digitalis; it was subsequently learned that she had received the drug in small amounts for several weeks immediately prior to her admission. On August 23, attempts were made to secure electrocardiograms, but the wiring to the ward was defective and only Lead III could be obtained. (She was in a ward not then provided with elevator facilities, and it was regarded as unwise to move her down the stairs to the laboratory on a stretcher, as would have been necessary to secure proper records.) The one record that was obtained on

that day, however, showed normal A-V conduction and infrequent ventricular premature beats; so digitalis was started in doses of 0.2 gm. of the powdered leaf twice a day. She received this dose for the five days beginning with August 23 except for a single dose, which was reduced to 0.1 gm.; a total of 1.9 gm. in five days.

On August 26 it was noted that the heart rate was 160 per minute and apparently perfectly regular. The patient was vomiting but had no other symptoms

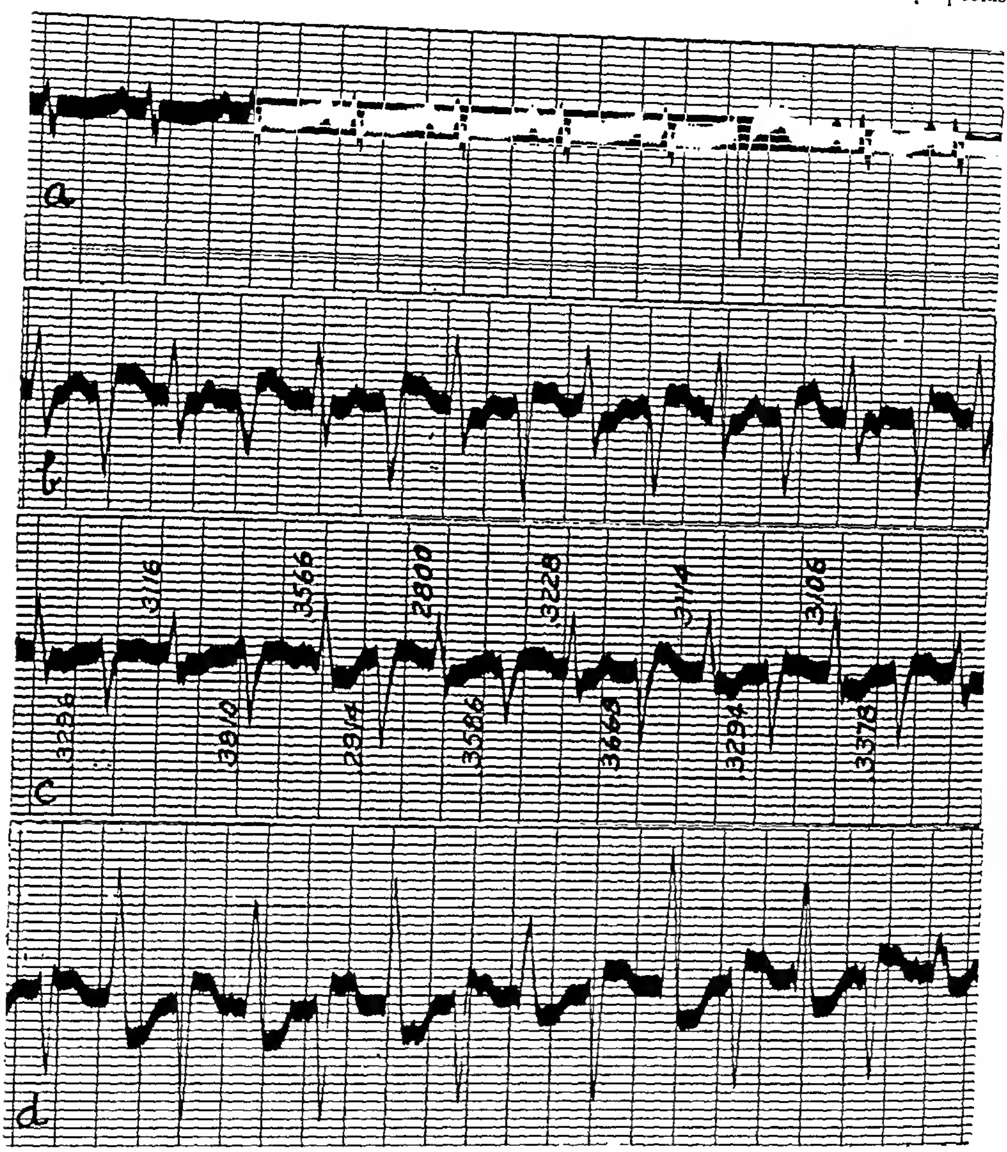

Fig. 8.—Case 3. The upper curve is of Lead III, taken Aug. 23; the lower three are the usual leads, taken Aug. 27. Auricular rate in the lower records is 200 per minute; ventricular rate varies from 171.4 to 184.6. The measurements in *c* are of the interventricular intervals. There are definite changes in form of occasional ventricular complexes, especially in Lead III.

of digitalis intoxication, and as she had been vomiting frequently for the two weeks before entrance to the hospital, as well as during the three days since entrance, this symptom was not regarded as significant. The rapid rate continued throughout the twenty-sixth and the twenty-seventh, so far as could be determined by frequent examination; it was not until the afternoon of the twenty-seventh that the electrocardiographic wiring was replaced and satisfactory records were secured.

Curves taken at that time revealed alternating ventricular tachycardia (Fig. 8); the probable rôle of digitalis was recognized, and the drug was permanently discontinued.

Vomiting continued to occur *frequently, but* it was apparently *not* due mainly to the digitalis, as it was present two weeks after all signs of digitalis effect upon the heart had disappeared. The original paroxysm of tachycardia ceased on August 28, but shorter paroxysms occurred with decreasing frequency during the two following days. None was observed thereafter until her discharge from the hospital on September 14, when she was in about the same condition as at the time of her admission. She died at her home two weeks later, apparently of congestive heart failure. Post-mortem examination was not performed.

Electrocardiograms.—In Fig. 8, *a* is shown a portion of Lead III, obtained on August 23, before the administration of digitalis was begun; it shows normal A-V conduction and a single premature beat arising in the ventricle. The three lower

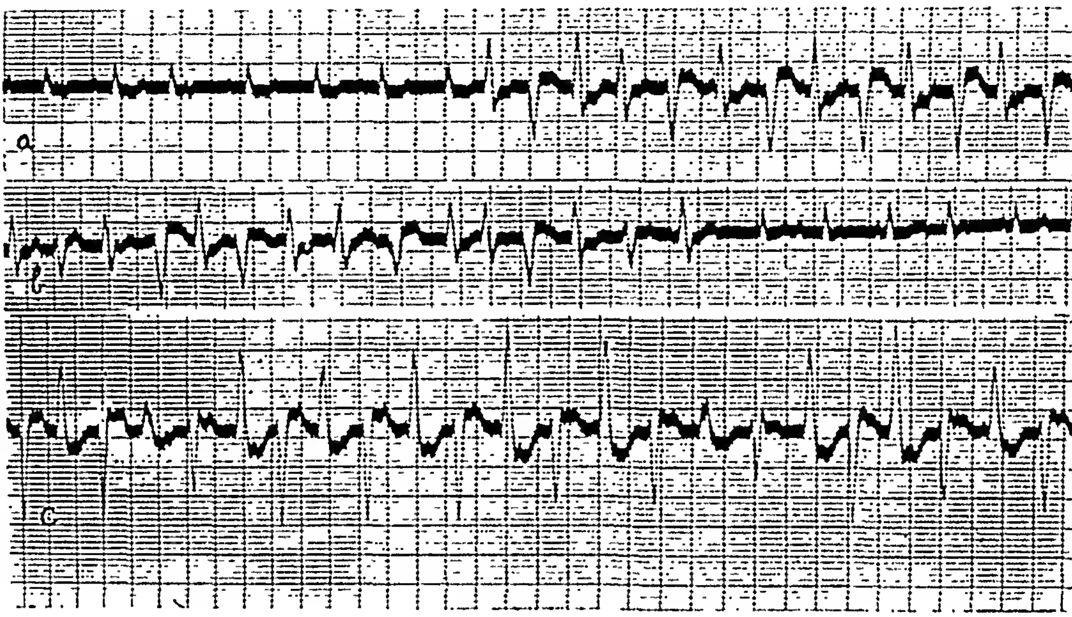

Fig. 9.—Case 3. *a* and *b* are from Lead I of two different curves taken on Aug. 28; they show the beginning and ending of a paroxysm. Partial A-V heart-block is present in the nontachycardial portions of these curves. *c* is from Lead III of the paroxysm that is shown beginning in *a*; note the occasional variations in size and shape of ventricular complexes. The auricular rate in Lead III is 203.2; the ventricular rate is from 190.8 to 193.4 per minute. (x 2/3)

curves are from one of the records of August 27 and portray the mechanism that apparently prevailed constantly for two and a half days—August 26, 27, and part of the twenty-eighth. Electrocardiograms were secured every few hours during the twenty-seventh and twenty-eighth, and the only differences in them were minor changes in the form of occasional ventricular deflections; changes that will be discussed presently. It is to be noted that there is both auricular and ventricular tachycardia, with complete dissociation of the two rhythms; the auricular rate is 200 per minute and that of the ventricles is from 171.4 to 184.6 per minute. Auricular waves can be clearly discerned in the central portion of Lead II and throughout most of Lead III.

On the evening of the twenty-eighth, the alternating ventricular complexes were not continuous; complexes of normal form were present in considerable numbers in response to auricular impulses, but with delayed A-V conduction. A selection

from a typical record of this period appears in Fig. 9, *a*, where the onset of a paroxysm is shown; partial A-V heart-block is present in the earlier portion of the curve. In the middle tracing of the figure, also Lead I, the offset of a paroxysm is registered, but from a record obtained some hours earlier than the upper curve. The lowest record of the figure represents the same paroxysm of which the beginning is shown in the upper record. The auricular rate during the paroxysms shown in

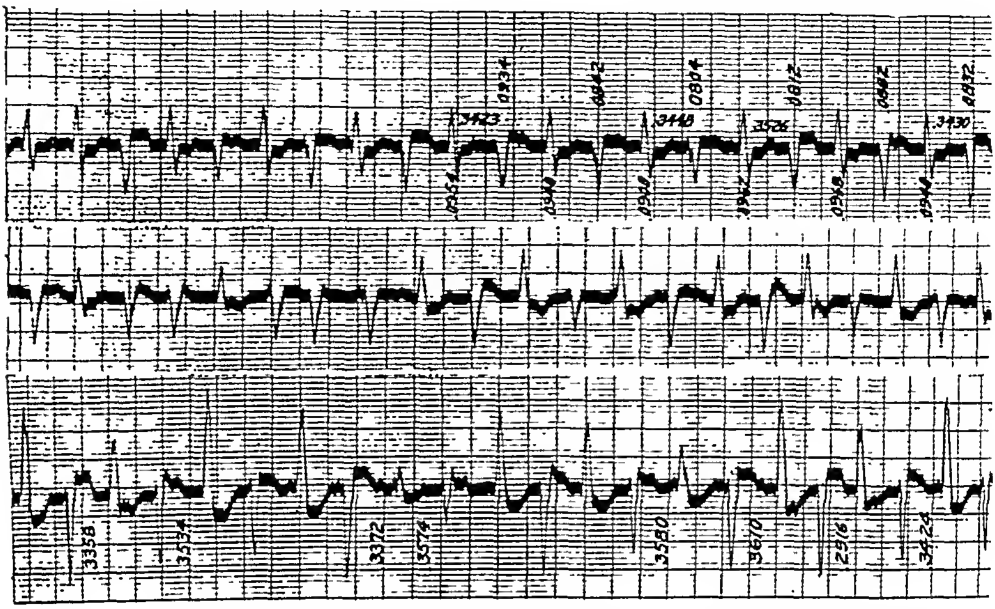

Fig. 10.—Case 3. Leads I, II, and III of one of the long paroxysms on Aug. 28. Measurements of the duration of ventricular complexes are shown in Lead I; the length of interventricular intervals is indicated in Leads I and III. It is to be noted that the degree of aberration of any complex bears no constant relation to the length of the pause preceding it. Auricular rate, 196.5 to 198; ventricular rate varies from 170.4 to 181.3 per minute. (x ⅔)

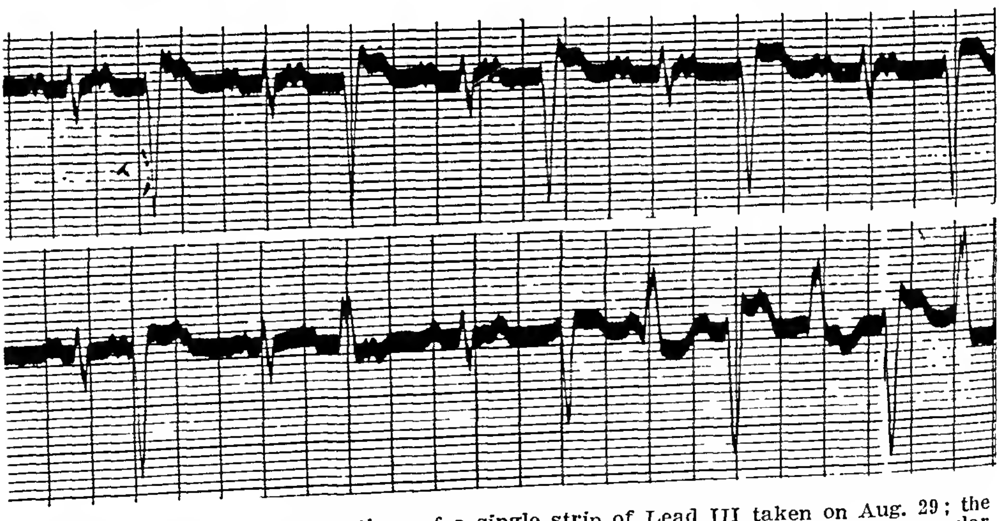

Fig. 11.—Case 3. Two portions of a single strip of Lead III taken on Aug. 29; the omitted intervening portion contained no ectopic beats. The upper curve shows regular coupling; the lower contains two ectopic beats and the beginning of a paroxysm of tachycardia composed of beats almost precisely like the preceding ectopic ones. The auricular rate is 200 per minute throughout; the ventricular rate during the paroxysm is 166.6 per minute.

this figure is from 196.5 to 200 per minute; the ventricular rate is from 183.3 to 192, the calculated rate depending upon the portion of the film chosen for measurement. The record displayed in *c* is inserted primarily to illustrate the differences in

the form of individual ventricular deflections that may occur without affecting the regularity of the alternation in direction.

Fig. 10 represents the three usual leads of an electrocardiogram obtained during one of the longer paroxysms. The change from an irregular to a regular alternation in the direction of the ventricular complexes is admirably shown in Lead II. Measurements of the actual duration of individual ventricular complexes are shown in Lead I; they are given for the sake of comparison with the measurements of the normal complexes in the same lead. The significance of the differences in the length of interventricular intervals, as indicated in Leads I and III, will receive comment in the later discussion. The auricular rate in this figure is from

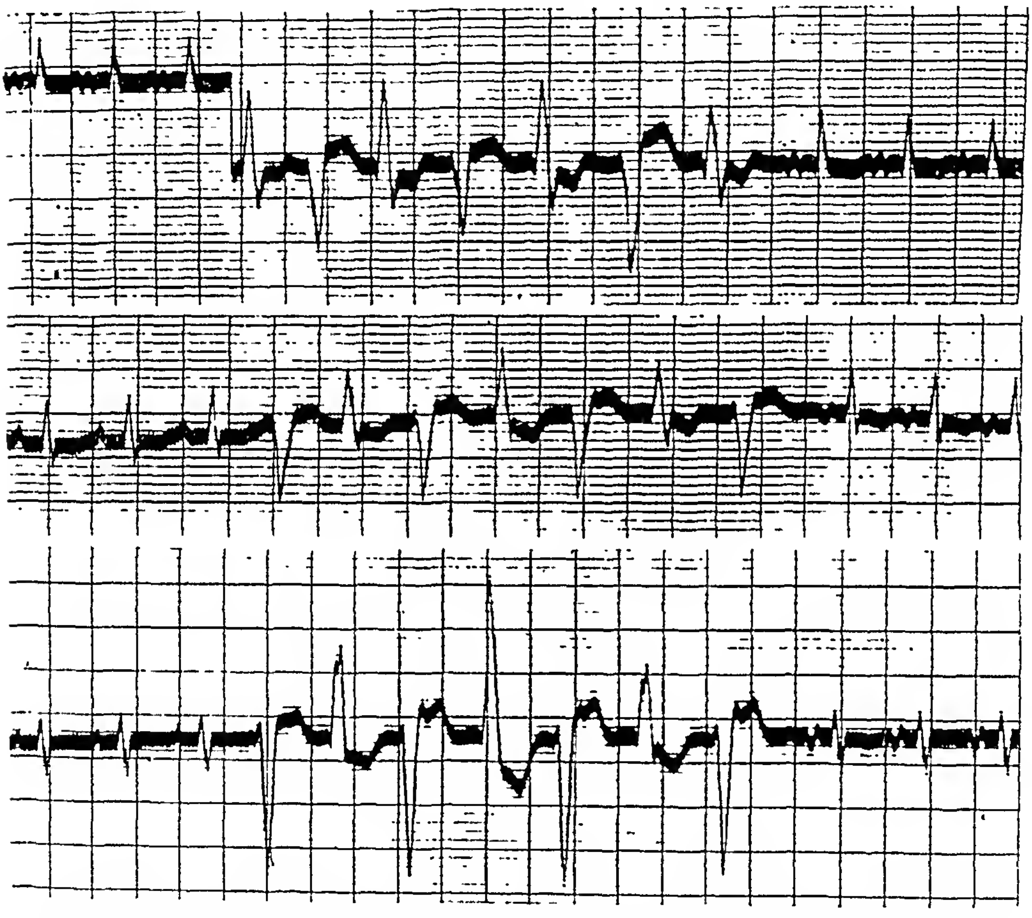

Fig. 12.—Case 3. Three usual leads. There is a brief alternating paroxysm in each lead. Note the change in the auricular waves after the paroxysm in Leads II and III. The initial beat of the paroxysm is clearly premature.

196.5 to 198 per minute; the ventricular rate is quite irregular and, in the measured portions, varies from 170.4 to 181.3 per minute.

Of considerable interest from the standpoint of the mechanism involved in the alternating tachycardia is Fig. 11. It represents two portions of a single strip of Lead III; five normal beats intervene between the two and are omitted to save space. In the upper curve there is perfect coupled rhythm, each normal complex being a response to each third rhythmic auricular impulse. The auricular rate is 200 per minute; the total ventricular rate is 128.5. In the lower half of the figure the second and fourth beats are ectopic, one of them identical with those shown in the upper curve and the other apparently arising in the opposite ventricle. The sixth complex of the lower curve ushers in a paroxysm of the alternating type,

and it is to be observed that the complexes which compose it are almost identical in form with the two ectopic beats preceding it. The auricular rate continues unchanged at 200 per minute throughout the paroxysm, while the rate of the ventricles at the onset of the tachycardia is 166.6.

Fig. 12 represents the three usual leads of an electrocardiogram obtained on August 30. A brief paroxysm consisting of seven beats is shown in each lead, and it is to be observed that the form of the auricular complex changes materially after the paroxysm in Leads II and III. The beat that initiates the paroxysm is in each instance clearly premature.

The final selection from the records of this patient is shown in Fig. 13. It represents the type of electrocardiograms obtained daily during the last two weeks of her stay in the hospital. In each lead ectopic ventricular beats are to be seen.

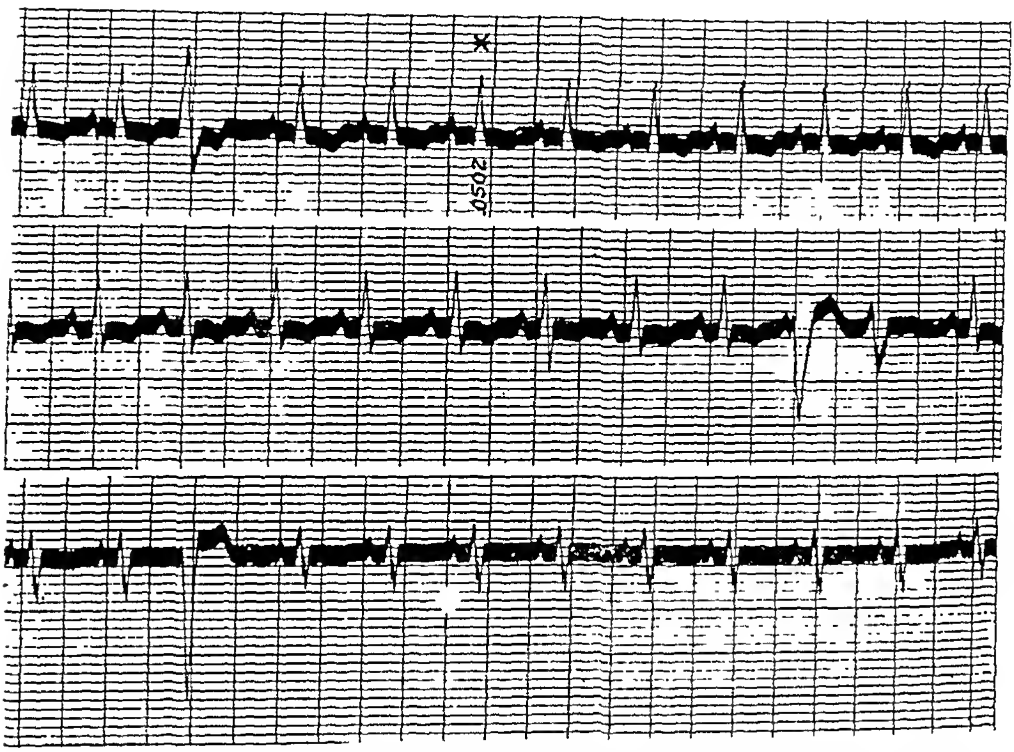

Fig. 13.—Case 3. Three usual leads, typical of the records obtained from Aug. 31 to Sept. 14. Normal mechanism with occasional ectopic ventricular beats. The complex in Lead I marked by an asterisk is the one measured for plotting as shown in Fig. 20. Note the striking *similarity* in form and size between the ectopic beats of this figure and those in corresponding leads during the paroxysms of tachycardia.

Comment.—The electrocardiograms obtained from this patient are of considerable interest. They may be described briefly as indicating a persistent tachycardia of both auricles and ventricles, with complete A-V dissociation, during the days when the action of digitalis was presumably at its height. During succeeding days the tachycardial periods became steadily less frequent and of shorter duration, and normal ventricular complexes began to make their appearance in response to auricular impulses, but there was partial A-V heart-block with dropped beats. (See Fig. 9, *a* and *b*.) This delay in conduction steadily became less, the responses to auricular impulses more numerous, until eventually normal mechanism was resumed, with oc-

casional ectopic ventricular beats. It is not proved, but seems extremely probable, that the events were related to the administration of digitalis and disappeared gradually as the drug was excreted from the body. The striking similarity between this case and that presented as Case 1 is worthy of emphasis; the same general comments might well serve for both.

CASE 4.—A woman, thirty-nine years of age, entered the hospital on November 23 because of shortness of breath and great swelling of the body and extremities. She stated that she was known to have had heart disease since the age of twelve or thirteen, but symptoms had appeared only two years previous to admission. For a year and a half there was dyspnea on exertion, but during the past six months edema had been present most of the time. She refused to restrict her activity until symptoms became so severe as to force her to remain in bed. During the past few weeks she had grown rapidly worse. The only fact of apparent significance in her past history was the occurrence of acute rheumatic fever in childhood.

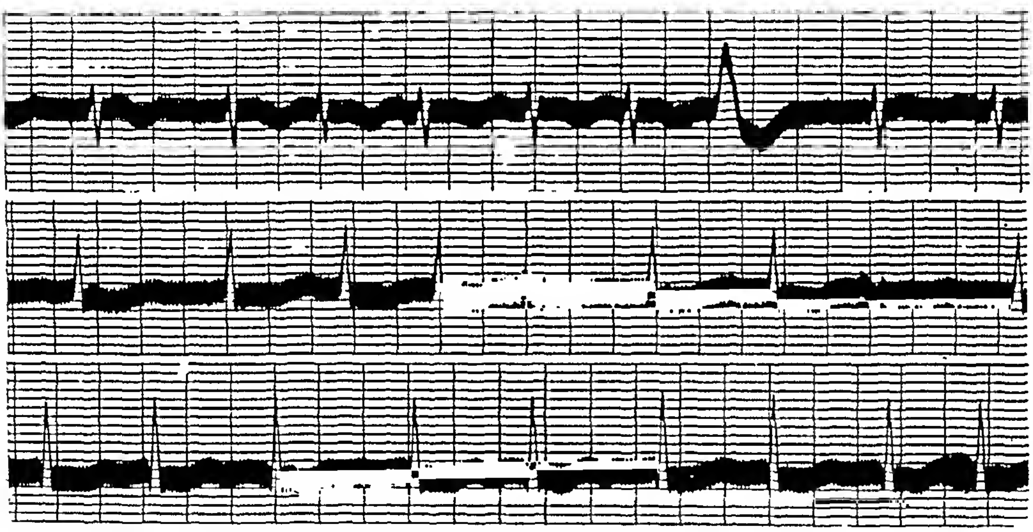

Fig. 14.—Case 4. Leads I, II, and III; auricular fibrillation, ectopic ventricular beats, right axis deviation, digitalis inversion of T-waves.

At the time of entrance to the hospital the patient was critically ill. There was extreme dyspnea, conspicuous cyanosis of lips and cheeks, and great engorgement of neck veins. The heart was considerably enlarged and presented the signs of stenosis and insufficiency of the aortic and mitral valves; the rhythm was totally irregular and the ventricular rate was approximately 150 per minute. There were signs of pulmonary and hepatic congestion, the abdomen was distended with fluid, and there was extreme edema of the lower trunk and lower extremities. The blood Wassermann reaction was negative.

Course and Treatment.—The patient was admitted at 1:40 A.M., Nov. 23. Her weight was 143 pounds. She received digifolin intravenously as follows: 5 c.c. at 2 A.M., 5 c.c. at 2:30 A.M., and 4 c.c. at 3 A.M., a total of 14 c.c., equivalent to 1.4 grams of the powdered leaf, within one hour. At 3:30 A.M., the heart rate had fallen to 78 per minute, and remained between 80 and 90 per minute until the afternoon of Nov. 24, when it was found to be between 90 and 100. She was therefore given 0.4 gm. of digitalis leaf by mouth at 8 P.M. On the following

morning the heart rate was found to be rapid and regular, and an electrocardiogram taken at this time showed paroxysmal ventricular tachycardia (Fig. 15) with a rate of 183.3 per minute.

From this time until her death three and a half days later there were frequent paroxysms of tachycardia, some of them lasting for several hours, most of them terminating abruptly after a few minutes. Between the paroxysms there was auricular fibrillation, with numerous ectopic ventricular beats. So far as could be determined by clinical observation, the patient was no worse during the long paroxysms than during the periods of auricular fibrillation with normal ventricular rate. Death occurred at 2:20 A.M., Nov. 29, two days after signs of pulmonary infarction had appeared over the right lower lobe.

Fig. 15.—Case 4. *a* and *b*, Lead I during and just after the usual type of paroxysmal tachycardia. *c* and *d*, Lead III showing onset and offset of a similar paroxysm. The isolated ectopic beats in Lead I are closely similar to those which compose the paroxysm in the same lead.

Autopsy.—There was extreme edema of the entire body except the face. There was a large quantity of free fluid in the abdomen and in both pleural cavities. The parietal pericardium was firmly adherent to the left pleura, the diaphragm, and the sternum; the pericardial sac was obliterated by adhesions. The heart with its attached pericardium weighed 630 gm. The wall of the right ventricle was 6 mm. in thickness: that of the left was from 16 to 18 mm. There was a large mural thrombus in the right auricular appendage. The tricuspid and pulmonary valves were normal. In the left auricle there was a huge thrombus, 1 cm. in thickness, covering the entire wall except the small portion leading into the

funnel-shaped mitral orifice; the thrombus extended into and solidly filled the greatly dilated left auricular appendage. There was advanced stenosis of the mitral orifice, the opening measuring 1 cm. by 0.5 mm., lying at the bottom of the rigid funnel typical of extreme stenosis. The tissues surrounding the slit-like opening were rigid and calcareous. The papillary muscles were greatly hypertrophied; the chordae tendinae were shortened and very thick. The aortic orifice was triangular in shape and measured less than 4 mm. in its greatest diameter. The valve cusps were fused and greatly thickened. The intimal surface of the aorta appeared normal.

Over most of the right lower lobe of the lung the pleura presented the picture of acute inflammation. The lung tissue of that lobe showed extensive infarction. The branch of the pulmonary artery supplying that portion of the lung was almost closed by a thrombus which extended for several centimeters along the vessel and was firmly attached to the wall.

The microscopic sections of the heart revealed both acute and chronic inflammatory processes in the pericardium. The muscle fibers were extremely hypertrophied, with irregular gigantic nuclei. There were small scattered areas of fibrosis. There was diffuse infiltration of the interstitial tissue, especially in the left ventricle, with mononuclear and polynuclear cells. Typical Aschoff bodies were present.

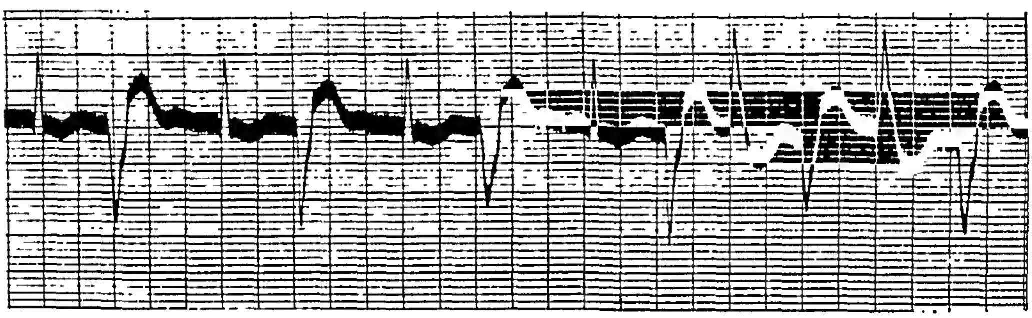

Fig. 16.—(x 9/11) Case 4. Lead III, showing a period of coupled rhythm followed by the onset of a paroxysm of tachycardia. The downward deflections of this paroxysm are almost identical in form and size with the preceding ectopic beats.

There was a widespread acute inflammatory process in and about the walls of the smaller coronary arteries, and a similar process in the wall of the left auricle; in this chamber, the inflammation extended to the endocardial surface, which was entirely covered by thrombus.

Comment.—In this case, as in the preceding one, we have to deal with paroxysms of tachycardia arising in ectopic foci and apparently bearing a definite relation to the administration of large doses of digitalis within a short time. Most of the recorded paroxysms in this case were of the form shown in Fig. 15; it is unfortunate that only a few beats of the alternating mechanism were successfully photographed, but there can be little question that the last few cycles of Fig. 16 represent the same type of abnormality as that shown in the preceding cases.

Case 5.—A man, seventy-four years of age, entered the hospital on May 15 because of weakness, difficulty in breathing, and swelling of the body and extremities. Symptoms had first been noted about four years previously, and had grown gradually but steadily more severe until one year before his admission,

when he had to abandon work. For the past nine months he had been forced to sit upright in order to breathe. During the several weeks immediately preceding his entry, he had become very much worse.

Examination showed extreme cyanosis of face, hands, feet, and mucous surfaces. There was orthopnea and dyspnea, and a frequent productive cough. The heart was greatly enlarged, the apex impulse being in the anterior axilla in the sixth intercostal space, and the right border of percussion dullness 4 cm. to the right of the median line in the fourth intercostal space. The rhythm was regular, the rate 100 per minute. There was a soft systolic murmur in the region of the apex. There was advanced sclerosis and tortuosity of the peripheral vessels; the blood pressure was 190 mm. Hg. systolic, 110 mm. diastolic. There were signs of congestion at the bases of the lungs, the liver edge was 8 cm. below the costal border in the right midclavicular line, and there was evident ascites. The entire body below the level of the lower ribs was extremely edematous. The blood Wassermann

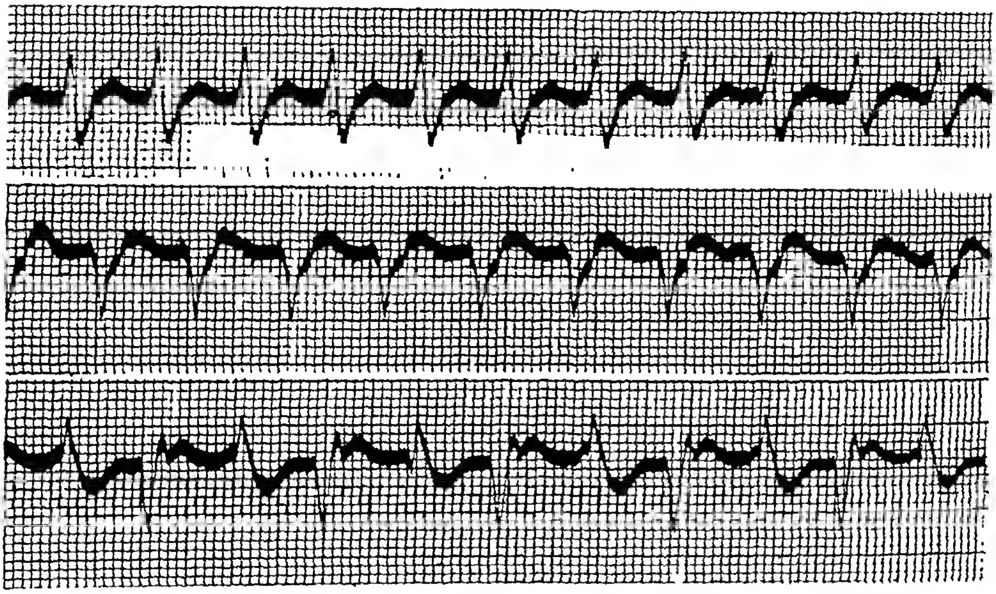

Fig. 17.—Case 5. Three usual leads. Alternation in the direction of the ventricular deflections occurs in Lead III only. Auricular waves cannot be discerned. The ventricular rate is 150 per minute in Lead I, 144.4 in Lead II, and 156.52 in Lead III. No records were obtained from this subject after the conclusion of the tachycardia.

was negative. The clinical diagnosis was arteriosclerosis and hypertension with heart disease; advanced congestive heart failure.

Course and Treatment.—The patient was admitted late in the afternoon of May 15. His weight was not determined; it was estimated at about 160 pounds with edema. He received the tincture of digitalis by mouth as follows: May 15, 9 c.c. at 8 P.M., and 4 c.c. at midnight; May 16, 4 c.c. at 4 A.M., at 8 A.M., and at noon: a total of 25 c.c., equivalent to 2.5 gm. of the powdered leaf, within a period of sixteen hours. Late in the afternoon of May 16, the heart rate was noted as very much more rapid than it had been in the morning; the tachycardia was still present on the following day, and an electrocardiogram was obtained (May 17). It showed, in Lead III only, the alternating type of tachycardia with which this paper is concerned. Leads I and II of that figure are regarded as probably indicating paroxysmal ventricular tachycardia, although they might equally well represent paroxysmal tachycardia of junctional origin; the widening and notching of the ventricular complexes in that event would be regarded as indicating pre-existing bundle-branch block or as due to aberration induced by the

rapid rate. Unfortunately, no record was obtained before or after the tachycardia, so no decision as to the nature of the mechanism is possible. The rapid rate continued apparently without change, until the evening of May 17, and was again present for several hours on the day following.

The patient grew steadily worse and died on May 20. Permission for postmortem examination was not granted.

Comment.—The study of this patient was far from complete, but it has seemed desirable to include his record with the others because it serves to emphasize the same time-relationship between the administration of digitalis and the onset of paroxysmal tachycardia of a very unusual type. An elderly man, he received an amount of digitalis greatly in excess of the calculated requirement, and received it within an extremely short time. A few hours later the heart was being driven by a new mechanism which persisted for the better part of two days. It is not known whether this new mechanism was of the alternating type most of the time, or whether alternation occurred only infrequently; nor is it a matter of great consequence. The important fact is that in this patient, as in the four preceding ones and in all similar recorded cases, the alternating type of ventricular deflections occurred during paroxysms that were apparently induced by large doses of digitalis. The complete evidence will be considered in a moment.

DISCUSSION

As stated earlier, the chief reason for placing the accompanying curves on record is that they appear to yield information as to the nature of the tachycardia. We are now in position to consider briefly the important features of the electrocardiograms and to summarize the evidence they provide as to the location of the pacemaker during the periods of tachycardia with regular alternation of upward and downward ventricular deflections. It is to be reemphasized that we are not now concerned with other forms of ventricular tachycardia, such as that shown in Fig. 15, nor with other disturbances of rhythm that may prevail occasionally in the same patients, except in so far as they serve to throw additional light upon the main point. The curves reproduced have been selected from the large number available in an effort to illustrate the origin of the new mechanism rather than the numerous minor differences that may occur from day to day in the form of the ventricular deflections during such paroxysms. It is recognized that Case 5 has no importance in this respect. The following discussion is based, therefore, largely on the first three cases presented; the last two have been included because they strengthen the evidence in respect of the rôle of digitalis. The evidence will be discussed as a whole instead of separately for each patient.

It seems clear that the impulses responsible for the rapid ventricular rate may conceivably arise either within or above the ventricles.

If within the ventricles, they are presumably generated alternately in right and left chambers; if above the ventricles, they are presumably transmitted alternately over right and left divisions of the bundle, with partial or complete blocking of transmission over the other branch. These two possibilities have been recognized by all who have discussed the matter[5, 6, 7]; there is a third one which will be considered later.

Now the form of the ventricular complexes during these paroxysms is very similar to, and in many instances identical with, that of ectopic beats arising in the ventricles, rather than with the complexes seen in instances of known bundle-branch block. The total duration of the ventricular deflections is frequently within normal limits, and *there may be complete absence of the characteristic notching* observed in the clinical curves of bundle-branch lesions, and regarded as indicating spread of the impulse to the homolateral ventricle. This fact has been mentioned by Felberbaum as an argument against a supraventricular origin of impulses. But the argument rests upon the assumption that there is *complete* blocking of impulse transmission alternately on right and left sides, and it is far from certain that such an assumption is justifiable. It may be assumed, with equal reason, that there is a delay in bundle-branch conduction, without complete blocking, due to lengthening of the refractory period of the branches, with consequent alternating preponderance of right and left ventricular effects. This possibility has been emphasized in connection with the examples of changing ventricular complexes in complete heart-block reported by a number of observers and thoughtfully discussed by Korns[8] and by Gilchrist and Cohn.[9] Korns concludes that the change from upward to downward ventricular complexes in his case of auricular fibrillation with high grade A-V heart-block is due to variations in the refractory period of the bundle-branches, a constant focus of impulse formation being above the bifurcation of the bundle; Gilchrist and Cohn regard the changes in the direction and form of ventricular complexes in their patients as due to a shifting of the impulse center from one side of the bundle division to the other. The experimental work of Wilson and Herrmann[10] strongly suggests that the latter explanation is the more likely one in cases where the changes in the ventricular complexes are associated with complete heart-block. A detailed consideration of the two views would carry us far afield and is not necessary at present, for the curves here presented afford definite evidence in favor of one of them. It is important to point out, however, that the evidence derived from the mere form of the complexes is not decisive.

An indication that the new pacemaker probably resides within the ventricles is found in the irregularity of rate during the maintenance of the paroxysm. Luten has argued, and logically, that the absolute

regularity of rate in his curves is in favor of a single focus of impulse formation, rather than separate foci in the two ventricles. The argument loses force if it can be shown that regularity is not an invariable, nor even a frequent, characteristic of the paroxysms. Paroxysms of tachycardia arising in the supraventricular tissues are notable for their regularity[11]; those arising in the ventricles are often slightly but distinctly irregular, as has been pointed out by several authors[3, 12] and emphasized by Strong and Levine.[13] Irregularity is a feature of practically all paroxysms registered in the patients here reported; in some of the accompanying curves the variation in interventricular intervals is sufficiently great to be apparent on casual inspection; in others, careful measurements disclose significant differences. (See Figs. 1, 8 *c*, and 10.) This irregularity is regarded as an indication that the ectopic impulses arose within, rather than above, the ventricles.

In the second place, curves obtained from several patients between paroxysms exhibit typical and unquestionable ectopic beats arising in one ventricle, and these beats are similar in form and size to those of the paroxysm which are in the same direction. The occurrence of beats which can be unhesitatingly identified as originating in the ventricle, and their close similarity to beats later occurring in rapid sequence, speaks strongly for a common site of origin of the two. This point has been emphasized by Robinson and Herrmann[1] as important in distinguishing between paroxysmal tachycardia arising in the ventricles and that arising in the supraventricular tissues; it has also been stressed by Felberbaum, whose patient showed isolated ectopic ventricular beats. Occasionally it is possible to compare, in the same lead, isolated ectopic beats and those which initiate a paroxysm of tachycardia; in most such instances (Figs. 3 *c* and 16) it is found that these single ectopic beats stand in the same relation to the preceding normal beats as do the initial beats of the paroxysm to the normal beats that precede them.

There is considerable variation, even in a short stretch of the paroxysm, in the form of the ventricular complexes, variations which might be thought to represent varying time-relations of the levo- and dextrocardiogram. These variations are usually not sufficiently great to permit the statement that they afford evidence of intraventricular origin of impulses, for similar alterations may conceivably occur when the ventricles are responding to supraventricular impulses if there are variations in the refractory period of the bundle-branches (Korns). In some of the curves, however, there are occasional beats which, while preserving their regularity of alteration, show such conspicuous alterations in form as to make it improbable that they arose in the same focus as those which stand on either side of them. (See especially Figs. 8 *d*, 9 *c*, and Lead III of Fig. 10.) If it is assumed that these

complexes all represent responses to supraventricular impulses, with alternate refractoriness of right and left bundle-branches, then the change in form of any beat should bear a fairly constant relation to the length of the time interval preceding it—in other words, the shorter the diastolic pause, the greater should be the change in the complex that terminates it. But this is not the case; some of the most extreme alterations occur after pauses as long as, or longer than, those which precede the unaltered complexes. This is true whether the time interval between successive complexes is considered, or only the interval between successive complexes in the same direction. This variation in form may be satisfactorily explained on the assumption that the beats arise alternately in the ventricles, but not always at precisely the same level of the conduction system; it is very difficult to explain it upon the assumption that they arise above the bifurcation of the bundle.

The second case provides additional evidence bearing upon the origin of the impulses during the paroxysms of tachycardia. This patient was known to yield curves characteristic of left bundle-branch block; numerous examples were obtained before and after the occurrence of the tachycardia, and all were alike. Now if it is assumed that the pacemaker during the tachycardia is above the bifurcation of the A-V bundle, it is necessary to assume further that impulses reach and involve the conduction system of one ventricle before that of the other, and that they do so in an alternating fashion. Expressed otherwise, the assumption is that the first impulse reaches the left ventricle before it does the right, the second reaches the right ventricle before it does the left, and that the stimulation continues in this manner. This is a vital and inevitable part of any explanation that assumes the location of the pacemaker above the bifurcation of the bundle, for the initial portions of alternate complexes in these curves represent right and left ventricular effects. But in this patient it is impossible for any impulse originating above the ventricles to reach the left ventricle before it does the right, because, in the presence of left bundle-branch block, such impulses can reach the left ventricle only by *spreading* through the interventricular septum from the conduction system of the right ventricle. The only conceivable manner in which the left ventricle can be involved *first* is for the impulse to originate in that chamber below the level at which the bundle-branch is injured. That this is the probable event is also indicated by this consideration: the average duration of the ventricular complex of this patient when the heart is responding to sinus impulses is approximately 0.11 second (Fig. 5). This figure may safely be taken as indicating the least possible time in which an impulse can pass through the conduction pathway of the right ventricle and spread through the septum to involve that of the left; if

the time is altered by rapid beating it will be increased rather than shortened; a known and frequent effect of simple paroxysmal tachycardia is to widen the ventricular complexes. Yet it is found that the ventricular deflections during the paroxysms of tachycardia in this patient are of much shorter duration than those during the normal sinus rhythm; by actual measurement they average approximately 0.08 second, or about 0.03 second less than the nonparoxysmal beats in the corresponding lead (Fig. 6). This is a conspicuous and significant decrease; it can be explained in but one way, namely, that impulses are arising within the ventricles.

The occurrence of auricular waves during paroxysms of tachycardia, distinct from and at a slower rate than the ventricular complexes, has been mentioned not infrequently since the appearance of Robinson and Herrmann's paper[1] as an indication that the paroxysms in question are of ventricular origin. It may certainly be regarded as an indication that the paroxysm did not arise in the auricle, but it is by no means clear that the presence of auricular waves excludes the possibility of origin in the junctional tissues. For this reason, and because the question of auricular origin has not arisen in connection with any case of alternating ventricular tachycardia, no emphasis has been laid upon the occurrence of rhythmic auricular summits in the present curves.

There is a final test which may be applied in an effort to determine whether the ventricular complexes in these electrocardiograms represent beats arising in the ventricles, or aberrant responses to supraventricular impulses. Lewis[14] has shown that the normal ventricular complex is a summation of right and left ventricular effects; that if these effects are separated by producing first a temporary block of the right bundle-branch and then of the left, the algebraic summation of the corresponding electrocardiographic curves will yield complexes identical in all important respects with the normal ones. In order to apply this test it is necessary to plot out the complexes accurately to scale. This has been done for the curves of Cases 3 and 2; the method is sufficiently indicated by Figs. 18, 19, and 20. The third and fourth ventricular deflections from the right-hand end of Lead I in Fig. 8 have been carefully and repeatedly measured by means of a comparator, and plotted to scale as shown in Fig. 18, *A* and *B*. The complex resulting from their algebraic summation in their presumably normal time relations is shown in Fig. 19, and is to be compared with the outline of the known normal for that lead, shown in Fig. 20. The measured normal complex is the third one following the ectopic beat in Lead I of Fig. 13; it is marked by an asterisk. The wide divergence of the two outlines needs no comment.

But it is not sufficient thus to summate the plotted figures in their apparently normal time relations; they must be shifted with refer-

ence to each other to ascertain if any possible combination of the two will result in a complex of normal outline, for if there is merely a delay in conduction along the bundle-branches, instead of complete block, the complexes will represent advancement or retardation of the levo- or the dextro-cardiogram. The procedure is made clear by the figures given in the paper of Gilchrist and Cohn.[9] These further steps have been carried out in detail but have not been illustrated. It will suffice to say that the plotted outlines have been

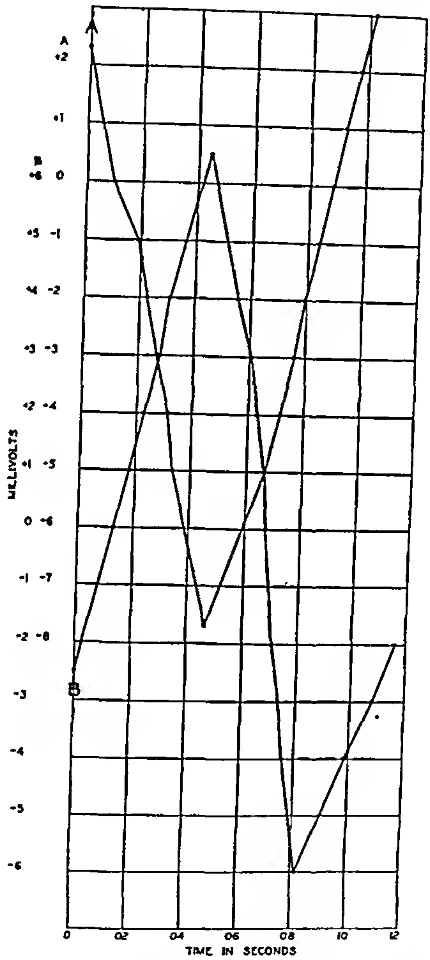

Fig. 18.—Typical upward and downward ventricular complexes of the paroxysms of Case 3 have been redrawn to scale. *A* represents the fourth complex from the right hand end of Lead I in Fig. 8; *B* represents the one immediately following.

moved with reference to each other so that first the levo-cardiogram and then the dextro-cardiogram took precedence, the shift being 0.02 second at a time, until the divergence from the normal became steadily greater. It was found impossible to arrange them in such a relation that their summation resulted in an outline resembling the normal.

The same procedure has been followed with the deflections of Figs. 5 and 6, although it seemed clear for the reasons already given that these ventricular complexes could not represent responses to supra-

ventricular impulses. It was again found impossible to place the plotted outlines in any relation such that their summation would yield the widened complex representing the invariable response to supraventricular impulses in this patient.

The complexes in Fig. 1 have not been similarly plotted because it is clear at a glance that the actual value of the downward deflections in Lead I is much greater than that of the upward deflections; it is impossible that their algebraic summation should result in a purely

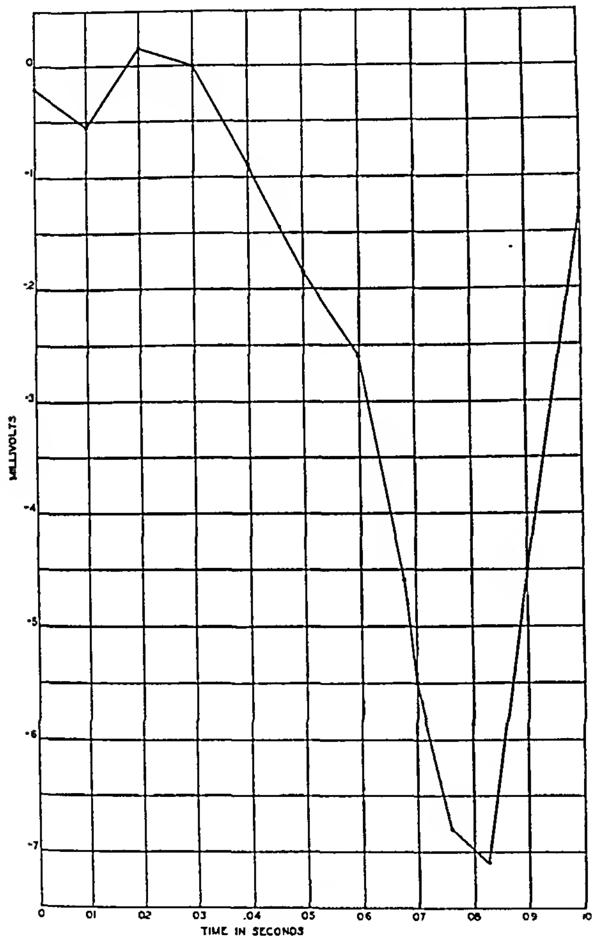

Fig. 19.—The curve which results from the algebraic summation of the outlines in Fig. 18 in their presumably normal time relationship. This is to be compared with the known normal complex for this lead, shown in Fig. 20.

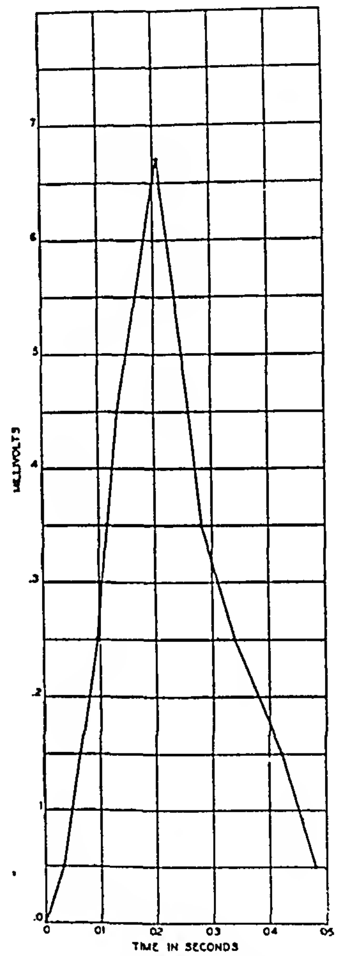

Fig. 20.—A normal complex of Lead I of Case 3 redrawn to scale. The actual complex chosen is that indicated by an asterisk in Fig. 13.

upward complex, no matter how the two outlines might be placed with reference to each other. Yet the known normal complex for this lead is an upward one (Fig. 4). Precisely similar arguments apply to Lead III of Fig. 1, in which the net value of the upward complex is nearly three times that of the downward one. The two measurements cannot possibly combine in such a way as to produce a downward complex; yet the known normal for this lead is downward.

For the reasons just given, it is regarded as fairly certain that the ventricular deflections in these three patients do not represent either partial or complete blocking of supraventricular impulses in the bundle-branches, that is, they are not actually levo- and dextro-cardiograms, nor even a summation of the two in differing time-relations. This is important evidence that the impulses responsible for these deflections actually arise within the ventricles.

Nature of the Paroxysmal Tachycardia.—If the evidence just presented is accepted as indicating that the abnormal mechanism has its origin within, rather than above, the ventricles, there is a further possibility that requires consideration, although, being largely hypothetical, it need not receive extended discussion. It is that the mechanism responsible for this curious disorder is a circus movement in the ventricle; that there is a circulating wave of excitation, similar to that occurring in the auricle in cases of auricular flutter and auricular fibrillation, pursuing a path relatively fixed and constant through the ventricular tissue, but not necessarily in the same plane in different patients or in the same patient during different paroxysms. The possibility is suggested by several characteristics of the curves, but it is supported mainly by the following considerations. Levy and Lewis[15] have obtained, from experimental animals under chloroform anesthesia, curves precisely analogous to those illustrating the present paper and have stated that this type of rhythm preceded the onset of ventricular fibrillation by only a few seconds. In a later paper, Levy[16] again explicitly states that the tachycardia characterized by alternate upward and downward ventricular complexes (regarded by him as extrasystoles generated alternately in right and left ventricles) often terminates in ventricular fibrillation, and the actual transition from one to the other is clearly depicted in his Fig. 4. Furthermore, Reid[4] has published records from a human case illustrating alternating tachycardia followed within a few seconds by ventricular fibrillation; the actual transition was not photographed. The number of instances in which this alternating tachycardia has been recorded in either human beings or experimental animals is small, yet it seems clear from these examples that there is a close relationship between the tachycardia and ventricular fibrillation, and it is at least conceivable that they represent earlier and later stages of the same disorder. Now there are many reasons for believing that ventricular fibrillation is due to circus movement in the ventricle; the evidence in support of that belief is so strong that it has led to general acceptance; it is lucidly and convincingly summarized by Lewis,[17] and need not be repeated here. If alternating tachycardia is closely related to ventricular fibrillation, and fibrillation is due to circus movement, it is possible—even probable—that the tachycardia is itself due to the same mechanism. The comparative regularity of the complexes and their relative constancy of

form during the alternating tachycardia would make it necessary to regard it as more nearly analogous to auricular flutter than to auricular fibrillation; that is, the circulating excitation wave pursues a longer and more nearly fixed path in ventricular tachycardia than in ventricular fibrillation. There is apparently nothing in the accompanying curves or in the known facts regarding ventricular fibrillation inconsistent with the belief that both may be due to the same fundamental mechanism.

The suggestion has been made briefly by others[2] that paroxysmal ventricular tachycardia of the usual form (in which there is no alternation in the direction of the ventricular complexes) might be due to circus movement. The facts supporting such a belief have been marshalled and carefully considered by Lewis,[18] who concludes that the evidence is not sufficiently decisive to warrant a final statement. It is believed that the relationship between the *alternating* tachycardia and circus movement is a little closer than that between the usual paroxysmal tachycardia and circus movement, because in the former case the actual transition to ventricular fibrillation has been shown to occur.

The argument need not be pressed, for it has not yet been finally proved that ventricular fibrillation is in fact due to circus movement, although the evidence is so overwhelming as to admit of little doubt.

Rôle of Digitalis.—The part played by digitalis in the development of this abnormal rhythm may be indicated briefly. It is known that digitalis often causes ectopic ventricular beats as an early manifestation of intoxication; it is known that ectopic beats in such circumstances may be increased in frequency up to the point of regular coupled rhythm by continued administration of the drug; it is known that ventricular fibrillation may be provoked in experimental animals by its intravenous injection.[19] There is strong evidence that excessive doses often cause paroxysms of ventricular tachycardia of the type usually encountered, in which the complexes are of one form.[4] When these suggestive facts are coupled with the observation that in every instance here reported and in all those previously observed, the disturbance followed the administration of large amounts of digitalis, and that in one patient tachycardia disappeared when the drug was stopped, only to reappear when it was again given, there can be little question that this form of tachycardia owes its inception to the administration of excessive quantities of the drug.

The relation of the dose of digitalis to the body weight cannot be ascertained precisely in any of the five patients. If the theoretical amount required for therapeutic effects is calculated on the basis of body weights, according to the well-known method of Eggleston, it seems clear that excessive quantities were given to the patients presented as Cases 1 and 5. But these patients were weighed while

edematous; the actual body weight was estimated, and was thought to be not more than 115 and 140 pounds, respectively. The second and third cases had received digitalis before admission to the hospital, the exact amounts being unknown; the total dose, therefore, cannot be definitely stated. The weight of the fourth patient was probably 120 pounds or less, and she received 1.4 gm. of digitalis within a period of one hour, without apparent ill effects. A single dose of 0.4 gm. forty-one hours later was followed by paroxysms of ventricular tachycardia. Even if it is assumed that the total amount (1.8 gm.) was present and active in the body at one time, the dosage is not greatly in excess of the calculated requirement. It must be kept in mind that amounts as large as, and even larger than, those used in the present cases have been administered to other patients without the subsequent development of alternating ventricular tachycardia. Careful consideration of the doses and the circumstances in which they were used leaves the impression that there are probably factors other than the total amount of digitalis which may be responsible for the onset of the mechanism under discussion.

It is possibly of significance that all of the patients mentioned in the present paper suffered from advanced congestive heart failure; it may be questioned whether similar doses of digitalis would have precipitated tachycardia in hearts less severely injured. Whether the size of the heart is an important factor is not clear; it is possible that only enlarged hearts are capable of spontaneously originating and sustaining a mechanism thought to depend upon circus movement in the ventricle; that is suggested by the observations of MacWilliams[20] and of Garrey,[21] and by the fact that all recorded examples of the alternating tachycardia occurred in patients with very considerable enlargement of the heart.

It is of some interest that three of the five patients did not suffer from headache, nausea, or vomiting. The record of one of them does not mention these symptoms and presumably they were absent, but a definite statement is not warranted. These symptoms occur with such uniformity as early manifestations of intoxication that there is an apparent tendency to believe that digitalis may safely be given until they appear. Such a rule may possibly be followed with safety if the drug is given relatively slowly over a prolonged period; that it may be unwise when large doses are used is sufficiently shown by the present cases. Yellow vision, mentioned as an occasional toxic manifestation of digitalis, did not occur in any of the first four cases here reported; it is not known whether it was present in the fifth.

From the standpoint of immediate practical application, the implications are clear. Any significant increase in heart rate, without an obvious physiological cause, in a patient who is receiving digitalis, or

any apparent failure of digitalis to slow the fibrillating heart, should be regarded with suspicion. In either case, digitalis should not be continued until an electrocardiogram has been secured.

SUMMARY

Five cases are reported in which there occurred paroxysms of tachycardia of a most unusual kind. These paroxysms consisted of regularly alternating upward and downward ventricular complexes. Only five similar examples have been recorded previously.

Reasons are given for believing that the paroxysms are due to ectopic beats arising alternately within the right and left ventricles; the possibility that circus movement in the ventricles may be responsible for this abnormal mechanism is briefly discussed.

In all of the recorded cases, this curious ventricular tachycardia seems to have occurred as a result of excessive doses of digitalis, although the usual symptoms of intoxication may be entirely absent.

The author wishes to express his thanks to Dr. Alfred E. Cohn, who kindly read the manuscript and made many suggestions for its improvement, and to Miss Mabel Carmichael for the preparation of the electrocardiographic prints.*

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*Since this paper was written, Palmer and White (Am. Heart Jour., 1928, iii, 454) have reported two other cases of this type of ventricular tachycardia, and have mentioned the three cases of Gallavardin (Arch. d. mal. du Coeur, 1926, xix, 153) unfortunately overlooked by the writer in reviewing the previous literature. Apparently Gallavardin was the first to suggest the possibility of circus movement in the ventricle as an explanation of this unusual type of tachycardia: Palmer and White have brought forward evidence in support of that view. The present paper has been allowed to stand as originally written because the evidence here presented is quite different from that of Palmer and White, although leading to much the same conclusions.

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COMPRESSION AND DISPLACEMENT OF THE BRONCHI IN MITRAL STENOSIS*

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INTRODUCTION

ENLARGEMENT of the left auricle is a very common event in mitral stenosis. It may reach considerable proportions and as a result various complications from distortion of the upper mediastinal contents may occur; for example, paralysis of the left recurrent laryngeal nerve, compression and displacement of the esophagus, changes in the outline of the right border of the heart and stenosis of the left bronchus, and spreading of the angle of the departure of the bronchi from the trachea. In this paper I wish to discuss the last condition.

Recently a patient came under observation in whom the results of narrowing of the left bronchus, due to compression by an enlarged left auricle, could be demonstrated. Since this is a rather unusual complication of mitral stenosis the case is being reported in detail.

REPORT OF CASE

F. C., a white man, aged forty-seven years, was admitted to the Medical Service of the University of Chicago Clinics January 5, 1928, complaining of "shortness of breath and pain in the left side." The family history was unimportant. He had enjoyed excellent health until a decade ago when he suffered from an acute febrile illness which was diagnosed as influenza during the great pandemic. He had never had rheumatic fever.

Following this illness he began to notice palpitation and dyspnea on exertion. These progressed through a period of two years, when he was forced to seek hospital aid for several months. Following recovery, tonsillectomy was performed, and he remained well for three years. That winter (five years ago) he suffered an attack of "bronchitis"—cough, blood-streaked sputum and dyspnea—lasting for several months. Similar attacks have occurred each winter since and during one such attack two years ago, the second attack of decompensation occurred. He improved with rest in bed and with the administration of digitalis, which he has been taking off and on ever since, but constant cough, the expectoration of considerable amounts of sputum, dyspnea and edema in the evening have persisted. He has worked irregularly nevertheless up to the present illness.

Five weeks before admission sore throat developed, followed by rapid increase of dyspnea, cough, edema, and weakness. The amount of sputum expectorated increased notably, and became semipurulent in character. Two weeks ago chills and fever began and weakness forced him to bed. His condition slowly became worse until the day before admission a studden, stabbing pain in the left chest, augmented by respiratory effort, forced him to come to the hospital.

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Admission Physical Examination.—Temperature 101° F., pulse 120 at apex, 102 at wrist, both totally irregular. Respiration 42. He was an extremely ill, emaciated, dehydrated man, dyspneic and orthopneic with shallow, labored respirations and a constant cough accompanied by expectoration. There was slight cyanosis and no edema. The veins of the neck were moderately distended. The precordial region bulged, and the apical impulse was diffuse, yet forceful, in the fifth and sixth

Fig. 1.

left interspaces, 10.5 cm. to the left of the midline. A systolic and a long, rough diastolic murmur were present, the latter best heard in the third and fourth left interspaces to the left of the sternal margin. Limitation of motion over the left lower chest and retraction of the interspaces here were quite apparent. Percussion was normal over the right lung, but posteriorly below the scapula on the left there

was definite dullness. In this region were many fine and coarse moist râles, distant bronchial breathing and increased voice sounds. Elsewhere the respiratory murmur was normal, but râles of various types were heard over the whole chest, though not as numerous as at the left base. The liver was moderately enlarged. There was no ascites.

The urine contained moderate amounts of albumin and many hyaline and granular casts. There were 5,500,000 red blood cells per c.mm. and 15,000 white cells with a moderate increase of the polymorphonuclear leucocytes. The blood urea nitrogen and creatinine were normal. The Wassermann was negative, and blood cultures were negative. No tubercle bacilli were found in several examinations of the sputum, but numerous pyogenic cocci of many kinds were present. The six foot x-ray plate of the chest showed a large heart with enlargement of the curve between the aorta and left ventricle and secondary congestion of the lungs more marked on the left.

The clinical diagnosis was "mitral stenosis, cardiac insufficiency and bronchopneumonia at the left base."

Course.—The day following admission a friction rub appeared in the left axilla and frank tubular breathing was heard posteriorly. He was treated with digitalis, with rest in bed, and was given a sufficient amount of fluid. Steady improvement occurred, although for seventeen days a temperature of from 100° to 102° persisted. The lungs cleared slowly except the signs at the left base. Here impairment of the percussion note and moist râles remained, the breath sounds varied from complete suppression to an amphoric quality. The expectoration of sputum, mucopurulent in character, varied from 150 to 400 c.c. per diem.

After five weeks of these persistent signs the possibility of a unilateral, basal bronchiectasis, secondary to compression of the left main bronchus by the left auricle was suggested. Consequently lipiodol was injected into the trachea, and although evidence of bronchiectasis was lacking, the iodized oil clung rather neatly to the walls of the bronchi, disclosing a surprisingly wayward course of the left main bronchus. The natural downward convexity was disturbed by an upward displacement, beginning a few centimeters from the origin of the bronchus from the trachea, resulting in a somewhat S-shaped curve (Fig. 1). Marked narrowing was also apparent at this point. X-ray plates were then taken during deglutition of a thin barium mixture and these demonstrated a displacement of the esophagus to the right and backward.

Following the lipiodol injection, the patient again ran fever for a few days and was delirious. He soon recovered and was discharged much improved. At present he is still taking digitalis, leading a quiet but comfortable home life, yet cough with expectoration of 50 or 60 c.c. of sputum persists, together with some impairment of percussion and persistance of moist râles at the left base *only*.

COMMENT

The first report of cases of compression of the left main bronchus by an enlarged left auricle was made in 1838 by King.[1] He presented four cases which showed partial collapse of the left main bronchus at necropsy. Three of these were apparently cases of mitral stenosis, while the fourth was that of a child, two and a half years old, with "cerulean blue" cyanosis. The exact type of cardiac lesion is not quite clear. Anomalies of both the tricuspid and mitral orifices were, however, present. Both auricles were much enlarged and compression of a small part of the right main bronchus, as well as the left, had occurred.

In no case did compression reduce the lumen to more than one-half the original size, and King was of the opinion that, for this reason, pulmonary signs are not to be expected during life. He stated that the base of the left lung appeared, however, to contain less air than the right, that the bronchioles were filled with "turgid material" and that the whole base seemed partially solid.

Later in 1867, Friedreich[2] reported a case of high-grade mitral stenosis in a young girl who had "distention" of the lower part of the thorax on the left side and high-pitched inspiration and expiration over the left lung base, particularly near the hilus. These signs had persisted for several years when in 1850 he made the diagnosis of compression of the left main bronchus, four years before her death. The diagnosis was confirmed at necropsy by Virchow in 1854.

In 1889 Taylor[3] reported the necropsy of a boy of sixteen with a history of heart failure of three years' duration, clinically diagnosed mitral stenosis. No mention is made of lung signs. The heart was very large, particularly the left auricle which held eleven ounces of clotted blood. The mitral orifice was but a slit. The left bronchus was markedly flattened in an anteroposterior direction, running posterior to, rather than above, the left auricle. The changes in the lungs were described as follows: "The upper lobe (left) was retracted, showing brown induration. The lower lobe was collapsed—the upper two-thirds being almost airless, the lower two-thirds choked with coagulated blood." The right lung was merely edematous.

Between the time of this report of Taylor's and the beginning of the more careful study by German and Austrian workers, scarcely any mention of this phenomenon can be found. Two references to such condition are noted in English textbooks, however. The first is by West[4] who, very briefly, states that the anatomical relation of the left auricle to the bronchus makes it possible that enlargement causes pressure on the bronchus. The other is found in Allbutt and Rolleston's *System of Medicine* in the article by Sansom.[5] The description here is clear-cut and concise and is therefore quoted:

"The left auricle is occasionally so much dilated as to cause obstruction of the left bronchus and thus lead to a series of morbid changes in the lung which result from its total or partial occlusion. These pass through the stages of hyperemia and edema until the final conditions of collapse and induration are reached." And again, "In an early stage the most important symptom is stridulous respiration, confined to the left side of the chest and sometimes accompanied by fine crepitations at the left base. After a time there is dullness to percussion without much change in fremitus on palpation, the probable explanation of which is, that, although the condensation of the lung which is going on, ought to exaggerate the fremitus, the diminished lumen of the bronchus interferes with access of sound vibrations. The

respiratory murmur, in this condition, becomes harsh, but stridor masks it. The latest stage shows absolute dullness with total absence of vocal fremitus while the respiratory murmur is obliterated. A considerable degree of retraction may be observed in such cases."

In 1910 Stoerk[6] made a careful study of the anatomical relations of the mediastinal contents, particularly of the relations af the chamber of the heart to the main bronchi. He demonstrated the fact that the left auricle made up the posterior and superior parts of the heart and that the bifurcation of the trachea and main bronchi were in close relation just above it, the left main bronchus normally resting on the upper surface for a short distance.

He took measurements of previous observers, Aeby, von Hovorka and Kobler, concerning the angles of departure of the bronchi from the trachea, confirmed them and incorporated them with his own figures into a final estimation of the normal angle. Then in eight cases of mitral stenosis, he showed that the average of the angle of deviation was increased 30°. The minimal deflection in the group of cases of mitral disease was about that of the maximal in normal individuals. He also noted that compression of the left main bronchus occurred frequently.

Two years later Kahler,[7] by bronchoscopy, demonstrated during life a narrowing of the lumen of the left main bronchus in all of thirteen cases of mitral stenosis obtained for study from Kovac's clinic. In one case it was so marked that on bronchoscopic examination the opening through the compressed area appeared only as a slit-like orifice 2 mm. in width. He also measured from the point of view of bronchoscopy, the upward deviation which occurred. In one of these cases signs of "lung compression" at the left base were noted clinically. Two of these cases came to autopsy, and the compression found by bronchoscopic examination was present. Still more recently, Gabert[8] has confirmed these observations of displacement and compression by x-ray, but makes no statement as to the condition of the lungs. His is the first x-ray diagnosis of upward displacement of the left main bronchus. He photographed the chest in lateral and anteroposterior views, increasing somewhat the ordinary exposures for heart shadows, and was able to trace the air containing main bronchi dimly. It was quite evident that spreading of the bronchi occurred in the cases of mitral disease, when compared to his normal roentgenograms.

Quite recently Shaw[9] dealing with enormous dilatation of the left auricle to the right, mentions the clinical findings of consolidation of the left base and profuse expectoration without comment. Shaw[9] and Bramwell[10] also note some displacement of the trachea to the right in the same type of case. The amount of displacement to the right should be carefully measured, however, before assuming that displacement has occurred, since Kahler[7] noted that in from 57 per cent to 75 per

cent of normal individuals the lower portion of the trachea lies slightly to the right of the midline.

Schrötter[11] discusses a cause of elevation of the left bronchus, remote from the present condition, where effusion into the left chest has occurred. This is probably due, he believes, to the fact that the left lung and components are floated or pushed upward, causing rotation of the trachea and bronchi to the left, and not necessitating a widening of the angle of departure. In his second case, pleural effusion on the right side reversed the process; the right main bronchus was pushed up and the left one was lowered.

SUMMARY

In summary, then, bronchial compression by an enlarged left auricle has been known to occur for nearly a century. It is known also that due to this cause compression does occasionally cause morbid changes in the lung, recognizable clinically. The knowledge of this phenomenon may be of use in explaining persistent pulmonary signs otherwise puzzling. At present I believe that compression and displacement of the left bronchus are much more common in mitral disease than is supposed, but only infrequently are they great enough to give rise to secondary lung changes, such as bronchiectasis, chronic basilar infections, and atelectasis. I hope shortly to show that it may also be demonstrated by x-ray examination when no pulmonary signs exist.

The present case gave no evidence of bronchiectasis by x-ray examination, but the bronchial tree was outlined and the compression and displacement of the left main bronchus were apparent. This explains readily the persistence of the expectoration of sputum and of the abnormal pulmonary signs at the left base alone.

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THE EXTRACARDIAL NERVES—III*

Further Observations Upon the Relation of the Extracardial Nerves to Heart-Block

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It was found that accelerator nerve section caused circulatory failure if complete heart-block was present the location of which was in the ventricle, and that stimulation of the accelerator nerves prevented this.[1] Some other effects of extracardial nerve activity associated with these experiments and some minor problems related to them were considered of sufficient interest to report. The experimental conditions were like those of the previous report.

Effect of Accelerator Nerve Stimulation Upon the Heart Rate.—The effect of accelerator nerve stimulation upon the auricles was similar to that which occurs in the presence of the normal sinus rhythm (Table I). The effect upon the ventricles was an increase in the visible tone and force of contraction for a short time following the stimulation, and the action of the two nerves in this regard was the same. No increase in the ventricular rate followed the stimulation of either nerve as is the case in the intact heart, although the other characteristic effects of accelerator nerve stimulation were very striking. (Fig. 1.)

Table I

NO.	RATE BEFORE	AFTER STIMULATION RT. NERVE	OF L. NERVE
	A V	A V	A V
19	130/40	ineffective	172/42
20	120/56	220/56	200/56
58	139/39	200/40	170/40
62	140/56	300/56	240/56
63	140/39	200/40	200/40

Hering[2] and also Daly and Starling[3] obtained an increase in the rate of the ventricle by accelerator nerve stimulation in the dog and cat. Cullis and Tribe,[4] however, have also found that the sympathetic action on the ventricle was much reduced or absent (rabbit heart), although the usual auricular effect was produced. In many experiments a slow decline in ventricular rate was present, but accelerator nerve stimulation did not increase the ventricular rate above that just preceding the stimulation. For example, in one of the experiments, after the production of the block, the ventricular rate was 55

*From the Laboratory of the Faculty of Medicine in Paris.

per minute. Accelerator nerve stimulation did not increase it (215/55) [A V]. Fifteen minutes later the ventricular rate was 39 per minute and accelerator nerve stimulation did not affect it (200/40) [A V]. In three animals in which there was an excessive amount of accelerator

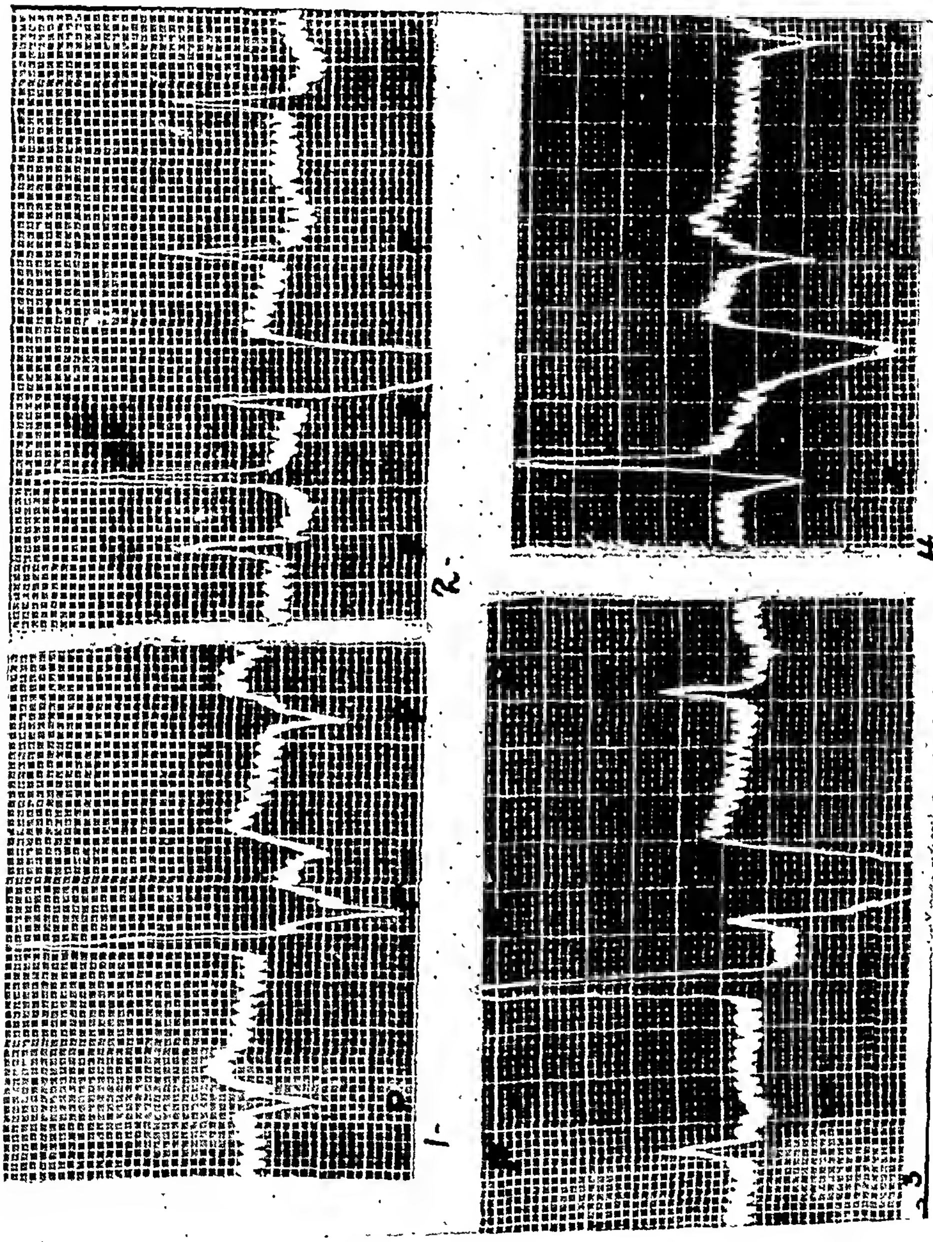

Fig. 1.—The effect of accelerator nerve stimulation in complete block. Axial (R.A.-L.L.) leading. Time in fiftieth seconds. (*1*) Auricular rate 152. The P-wave is inverted and followed by a positive P-T. This was constant during the half hour which preceded. (*2*) Just after stimulation of the right accelerator nerve. Auricular rate 190. The P-wave is positive, high, and followed by a negative P-T. Note the exaggerated effect upon the T-wave. (*3*) Ten minutes later. The auricular rate is 125. The other effects of accelerator nerve stimulation still endure. (*4*) After stimulation of the left accelerator nerve. The auricular rate is 125. The P-wave is again negative. The nega- [illegible]

nerve stimulation a gradual rise of the ventricular rate appeared which did not exceed the ventricular rate present at the beginning of the experiment. An illustration of this is the following—in one of the dogs after the production of the block the rate was 130/45 [A V] and thirty minutes later it was 130/24 [A V]. Following ten minutes' stimulation of

both accelerator nerves the highest ventricular rate obtained was forty-five per minute. Whether this slow rise in the rate was caused by the prolonged increase in the auricular activity rather than the direct effect of the accelerator nerves upon the ventricles could not be determined from these experiments.

The Effect of Adrenalin Upon the Block.—Adrenalin (0.1-0.2 c.c.) intravenously always resulted in the onset of ventricular fibrillation when it was administered in the presence of complete block. Small doses had no effect upon the ventricular rate.

The Electrocardiogram.—The electrocardiographic changes induced by accelerator nerve stimulation in complete block were similar to those which occur in the intact heart.[1] Right nerve stimulation caused increase in the height of the P-wave or if it was negative, caused it to become positive, and the left nerve stimulation usually caused inversion of the P-wave. (Fig. 1.)

The effect of the two nerves upon the T-wave was difficult to compare because the accelerator nerve stimulation very frequently altered the form of the QRS complex; and the T-wave changes induced were exaggerated and of long duration.

It appeared, however, as if the changes which accelerator nerve stimulation caused in the form of the ventricular curve were of the same character as those in the intact heart, stimulation of the left nerve tending to force the T-wave upward, and stimulation of the right nerve tending to force the T-wave downward, i.e., the effect of stimulation of each accelerator nerve upon the form of the electrocardiogram was qualitatively similar to that occurring in the intact heart. (Fig. 1.)

The Relation Between Vagus Stoppage and the Heart-Block.—The pre-automatic pause and the rhythm of development were constant in each heart and did not alter with the repetition of the block if recovery occurred. In one instance, recovery and reinduction of the block occurred seven times, and the length of the pre-automatic pause and the rhythm of development did not change. This was also the case after the accelerator nerves had been sectioned.

The duration of the stoppage of the intact heart induced by stimulation of the right vagus nerve was approximately equal to the length of the pre-automatic pause after complete block was established. When escape from stimulation occurred early, i.e., the duration of the stoppage was short, the pre-automatic pause was also short, and the onset of idioventricular rhythm was spontaneous and the rhythm of development was rapid. If no escape occurred during long stimulation of the right vagus nerve, the pre-automatic pause when the block was induced was always so long that rhythmic tapping of the ventricle had to be employed to hasten the onset of the idioventricular rhythm. This relation between the vagus nerve and the pre-automatic

pause has been observed by Erlanger and Hirschfelder.[5] When differences appeared between the duration of heart stoppage from vagus stimulation and the duration of the pre-automatic pause, the difference was one that favored the pre-automatic pause, i.e., the duration of vagus stoppage was less than the pre-automatic pause, which can be explained by the fact that stoppage of the heart from stimulation of the vagus nerve is broken by the autonomy of one of the points for impulse production, viz.—the S-A node, the A-V node, or the ventricles. Since the inherent rhythmic frequency of the first two is greater than that of the ventricles, the escape from vagus stimulation occurs sooner when it arises at either of these two points. Hence differences ought to be in the nature of a longer pre-automatic pause than vagus stoppage, which actually is the case.

There also was an inverse relation between the duration of heart stoppage during right vagus nerve stimulation and the time required for the appearance of the circulatory failure which followed the accelerator nerve section. Whenever the vagus effect was intense, there was a constant tendency for the time before death occurred following accelerator nerve section to be considerably shorter than where the escape of the heart from vagus stimulation was very prompt, differences arising so great as fifteen minutes for the one as against fifty minutes for the other.

Vagus Nerve Stimulation in Heart-Block.—The effect of vagus nerve stimulation upon the auricles was the same as that before the production of the heart-block, and no effect upon the ventricles directly attributable to the vagus nerve stimulation was observed. It was common to observe an after-effect of stimulation, an increase in the rate of the auricle and an increase in the tonus and strength of contraction of the ventricle. This was due to the sympathetic fibers which descend in the vagus trunk. It is of interest to note that the rhythmic stimulation of these fibers (by rhythmic stimulation of the vagus trunk after full doses of atropin) prevented the onset of the circulatory failure which appears after accelerator nerve section.

The Effect of Intact Vagi in Heart-Block When the Accelerator Nerves Are Sectioned.—In three animals the vagi were intact, and complete block was induced. In these the only effect of section of the vagi nerves was a small increase in auricular rate. In two other animals in which the vagi were intact, and block was induced, the accelerator nerves were sectioned. No difference in the usual effect occurred and circulatory failure ensued. Hence, the tonic activity of the sympathetic fibers which are contained in the vagus nerve trunk were not sufficient to prevent the circulatory failure and death which results from the accelerator nerve section, although strong and frequent excitation of these fibers did so.

The Relation Between the Ganglia Stellata and Rami Communicantes.—Singer[6] has studied the afferent (sensory) pathway for the nerves supplying the pericardium, the epicardium, and the first part of the aorta and has found that the reflex reaction to the stimulation of these parts is obliterated by the section of the n. rami communicantes of the C_8D_{1-3} spinal nerves. He has recommended the section of these nerves for the relief of cardiac pain as the alternative to removal of the stellate ganglia upon the ground that the afferent pathway only is broken. In three animals, after block was induced, the rami communicantes to these nerves were sectioned. The main sympathetic nerve trunk and the ganglia stellata were intact. There was no difference in the effects from those which occur when the ganglia stellata are removed. This suggests that the efferent (motor) pathway for the accelerator nerve is probably the same (n. ram. comm. C_8D_{1-3}) and that in so far as choice of operation is concerned no physiological distinction can be made between the resection of the ganglia stellata and the section of the n. rami communicantes C_8D_{1-3}.

SUMMARY

1. The effect of accelerator nerve stimulation upon the ventricular rate in complete block was found to be insignificant, although its action upon the form of the electrocardiogram is marked.

2. Adrenalin administered in the presence of experimental block caused ventricular fibrillation.

3. There is a relation between the effect of stimulation of the right vagus nerve, the pre-automatic pause of the ventricles and duration of life of the heart after accelerator nerve section.

4. The tonic activity of the sympathetic nerve fibers contained in the vagus trunk was insufficient to support the circulation in the presence of accelerator nerve section although stimulation of these fibers did so.

5. Section of the n. rami communicantes C_8D_{1-3} has the same effect as the removal of the stellate ganglia.

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THE EXTRACARDIAL NERVES—IV*

An Experimental Study of Coronary Obstruction

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INTRODUCTION

ALTHOUGH accelerator nerve section does not significantly affect the changes which follow many types of injury to the heart,[1] the important practical aspects of coronary closure suggested that it would be of interest to determine its relation to the extracardial nerves. The points investigated were the effect of accelerator nerve section and vagus nerve stimulation upon the closure of the coronary sinus and large and small arteries, and the associated electrocardiographic changes. Some of the observations included, although not directly concerned with the problem stated, are closely associated with it. Experimental studies upon the effects of coronary obstruction have been made by Lewis,[2] Smith,[3] Gold *et al.*,[4] and others. Danielopolu and Marcu[5] also studied the relation between the closure of coronary arteries and the accelerator nerves and have found that accelerator nerve section exaggerates the changes induced by closure of coronary arteries.

METHOD

The experiments were made upon dogs with chloretone narcosis, vagus nerve section, artificial respiration, opened chest and artificially maintained temperature. Axial electrocardiographic leading (R.A.-L.L.) was employed and where it was considered of interest other leads (R.A.-L.A. and L.A.-L.L.) were added. In twelve experiments the coronary sinus was ligated or clamped at the coronary dimple, before it opens into the cavity of the right auricle. After the accelerator nerves were sectioned there was an interval of one hour before the ligation. This length of time was suggested by other observations.[1] In the control animals the accelerator nerves were intact but the same interval was also allowed before the ligation. The same procedure was followed with the ligature of the arteries in 24 experiments.

RESULTS

Coronary Sinus.—The ligation of the coronary sinus did not completely obstruct the venous flow because of the venii Thesbesii, and occasionally this compensatory venous bed was large enough to allow a coronary circulation which prevented the death of the heart during the period of the experiment.

The immediate effect of the ligation of the coronary sinus was marked engorgement of the large veins and the appearance of many others not previously visible. This was followed by intense cyanosis

*From the Laboratory of Physiology, Faculty of Medicine, Paris.

of the surface of the left ventricle which did not, however, spread further anteriorly than the interventricular groove until death was imminent. The left ventricle enlarged and appeared functionless, hanging like a distended sac from the contracting portion of the heart, whereas the right ventricle retained its function and good color. At some time after the ligation (which varied from ten to fifty minutes), incomplete heart-block appeared. It was most often cyclic, i.e., it appeared first as a very high degree of block which passed into 2:1 block and it was then followed by 1:1 beating (recovery); and it slowly and irregularly repeated this cycle until death occurred. The auricle maintained its regular rhythm throughout and it suffered little alteration in its rate. No tachycardias and very few premature beats appeared during the course of the changes which finally resulted in death.

Post-mortem, the muscle of the external wall of the right ventricle was soft, whereas that of the left ventricle felt hard to the touch and was thicker than normal, and the cut surface oozed blood upon section. It was dark in color, and presented an appearance not unlike that which is seen with chronic passive congestion. The endocardial surface of the left ventricle including the septal wall was a purplish hue and appeared edematous, but that of the right ventricle including the septal wall was normal in color and appearance. The congestive discoloration extended into the septum about half-way through its thickness.

The Electrocardiogram.—The electrocardiogram of the axial lead presented an elevation of the T-wave. This positive effect upon the T-wave, although it occurred constantly, varied greatly in amount and time of onset, and no parallel existed between the electrocardiographic and the other changes occurring in the heart, since effects varied from an exaggerated early electrocardiographic change with delayed death to minor electrocardiographic change with early death (Table I). In two instances the R-T fusion appeared as the effect of the ligation (Fig. 1).

TABLE I

DOG	TIME BEFORE ECG CHANGE APPEARED	THE DEGREE OF CHANGE IN ECG	DEATH	ACCELERATOR NERVES
I	2 min	marked	15 min.	cut
II	3 "	"	50 "	"
III	15 "	"	25 "	"
IV	60 "	small	65 "	"
V	3 "	marked	21 "	"
VI	10 "	small	60 "	"
VII	3 "	marked	15 "	intact
VIII	5 "	"	35 "	"
IX	3 "	small	31 "	"
X	5 "	marked	no death	"
XI	no ECG		5 min.	"
XII	" "		no death	cut

There was no relation present between the heart rate, the effect of stimulation of the right vagus nerve and the effects of the ligature. The effect of accelerator nerve stimulation upon the altered electrocardiogram which the ligature induced was the same as under other conditions,[6, 1] right nerve stimulation lessening the height of the T-wave and left nerve stimulation increasing the height of the T-wave.

The Effect of Accelerator Nerve Section.—Accelerator nerve section did not influence the resistance of the heart to the effects of the ligature. Early death was equally common following the ligature when the accelerator nerves were intact as when they were sectioned and as many instances (one) in which the heart survived the ligature of the coronary sinus occurred when the nerves were sectioned as when they were intact. The nerve section did not influence the cyclic heart-block nor did it appear to effect the electrocardiographic changes which followed the ligature of the coronary sinus. The only effect

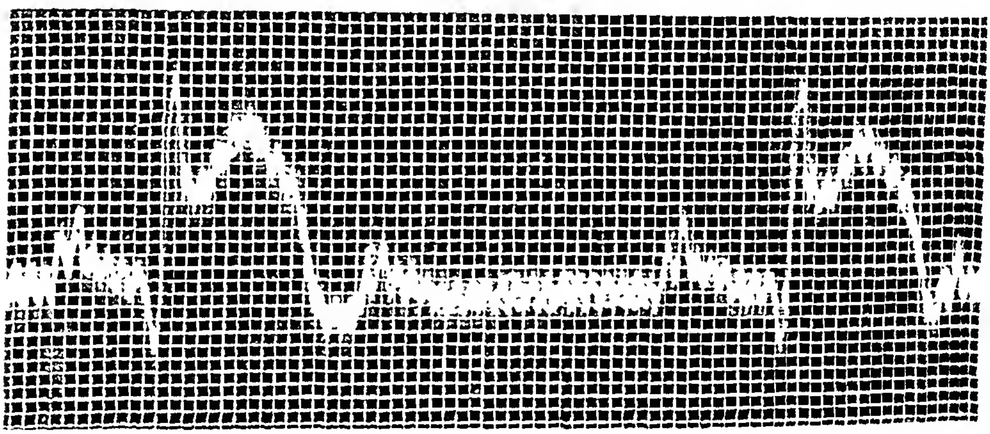

Fig. 1.—Axial (R.A.-L.L.) ECG. Time in fiftieth seconds. Ligature of the coronary sinus. A 2:1 heart-block and the RT fusion are present.

observed from the accelerator nerve section was in the manner by which the death of the heart occurred. When the accelerator nerves were intact, death occurred by the sudden onset of ventricular fibrillation. If the accelerator nerves were sectioned one hour before the ligature, the death occurred by diastole; i.e., a gradual dilatation of the right ventricle with a decrease in the muscle tone and strength of contraction.

Ligature of Coronary Arteries.—Twenty-four experiments were made. In all instances, shortly after the ligation, visible evidence of the effect appeared as a sharply demarcated discoloration of the area of heart muscle supplied by the branch ligated, associated with loss of function.*

Effect on Rate and Rhythm.—The ligature of small vessels caused no changes in the rate or rhythm but the ligation of large vessels

*A more detailed description of the events which follow coronary ligature is given by Lewis.[2]

caused a decline in the heart rate and was often followed by sudden variations in the rate which were phasically recurrent. The electrocardiograms were inconstant: some showed no alteration in the P-wave or P-R interval, other showed alteration in the form of the P-wave. These changes were probably related to the alterations of

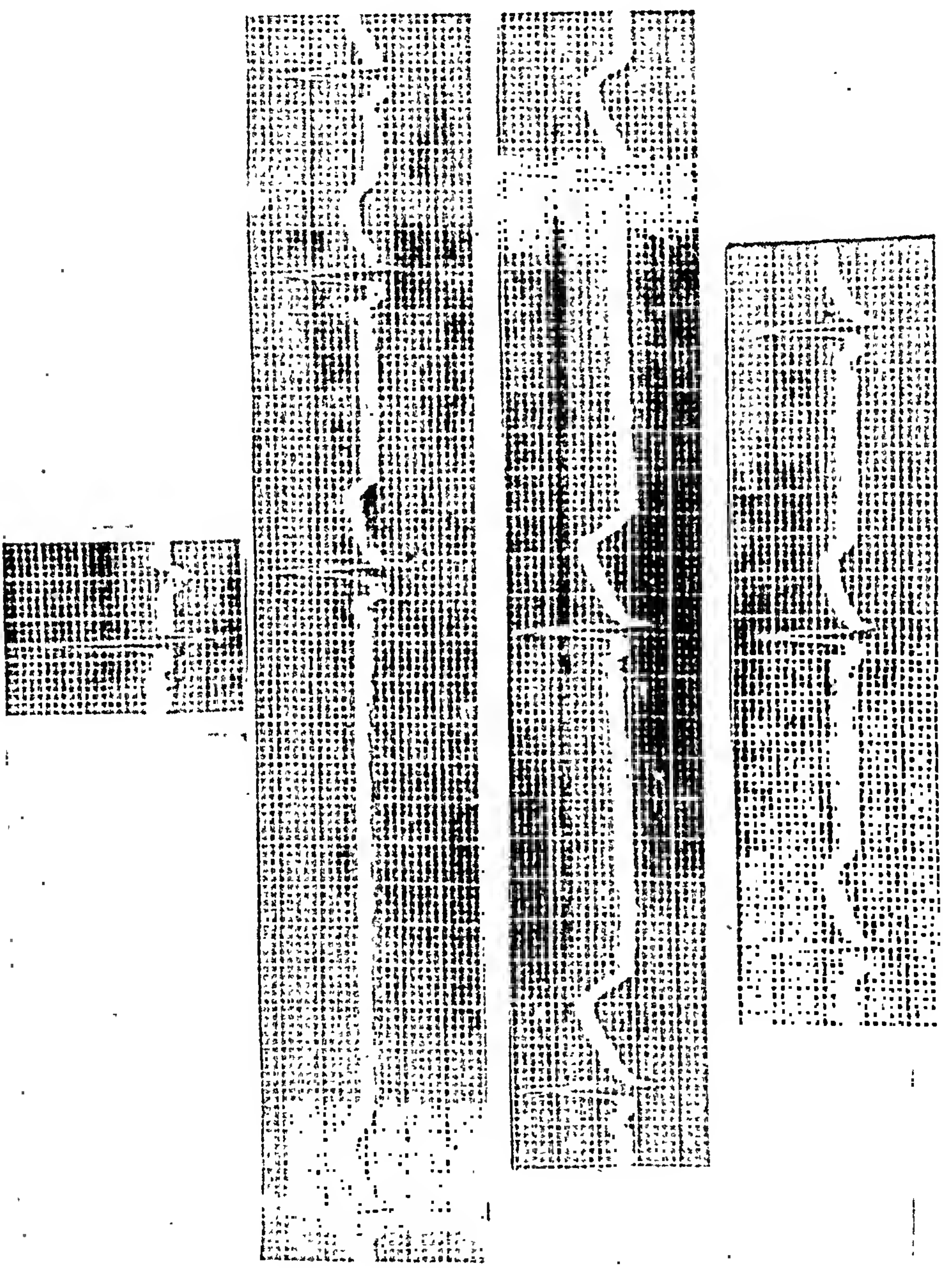

Fig. 2.—Axial (R.A.-L.L.) ECG. Time in fiftieth seconds. Ligature of the artery to the S-A node. (*1*) The normal sinus rhythm. (*2*) Complete irregularity in the rhythm which was the first effect of the ligature. (*3*) During a period of slow and regular rhythm (a slow phase). (*4*) During a period of more rapid and regular rhythm (a rapid phase).

the blood supply to the S-A node, since similar phasic variations in the rate of the auricles were observed after ligature of the artery to the S-A node (Fig. 2). They were also very common during the course of the heart failure which followed accelerator nerve section in heart-block,[1] and were occasionally observed to occur after section of all the extracardial nerves in the intact heart. These observations

suggest that nonrespiratory sinus arrythmia and sinus block are the effect of conditions which diminish the blood supply to the S-A node.

Ventricular premature beats were numerous and often recurred in groups. Lewis[2] noted that they appeared within from three to five minutes after the ligation in 7 of 17 animals. In these experiments they appeared later. The electrocardiographic form they assumed was mostly that of the right ventricular premature beat after ligation of the right coronary artery and of the left ventricular premature beat after ligation of branches of the left coronary artery.* Smith[3] has also noted the appearance of left ventricular premature beats after ligature of the descending division of the left coronary. Tachycardia was rare and it occurred in two of the twenty-four dogs; in one instance it was left ventricular tachycardia and followed ligation of the entire left coronary artery, ending with ventricular fibrillation. The other was nodal tachycardia, of short duration and irregularly recurrent

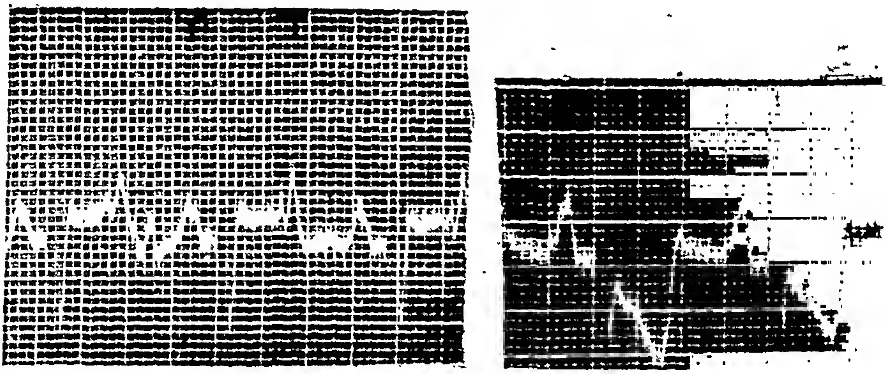

Fig. 3.—Axial ECG. (R.A.-L.L.) Time in fiftieth seconds. (*1*) Before ligation of the right coronary artery. (2) Ligature of the right coronary artery (ST fushion).

during the course of the experiment. It appeared after the ligation of the largest branch of the circumflex division of the left coronary artery.

The Electrocardiogram.—The ligation of the right coronary artery forced the T-wave of the electrocardiogram downward with a loss of the RT interval, and caused the ST fusion (Fig. 3). The ligation of the left coronary arteries forced the T-wave of the electrocardiogram upward with loss of the RT interval (Fig. 4, *a* and *b*). As in the case of the ligature of the coronary sinus, effects were constant in character but varied in the degree to which they occurred.

The RT fusion phenomenon was an inconstant occurrence after the closure of the left coronary artery. This has also been the observation of Gold *et al.*,[4] and others. However, the ligation of the second large branch arising from the circumflex division of the left coronary

*Concerning the question of interpretation of the electrocardiographic form of the premature beats, right and left, or basal and apical, either may be applied since the distribution of the right coronary artery is both to the right and basal portion of the heart and the left coronary artery, particularly its anterior division to the left and apical portions of the heart.

artery almost constantly resulted in the appearance of this form of electrocardiogram (Fig. 5). It supplies the external wall of the left ventricle on the posterior surface of the heart just above and to the right of the cardiac apex. When it failed to appear, the additional ligation of other branches from the branches of the anterior or circumflex divisions of the left coronary artery which may also supply this portion of the heart induced its appearance (Fig. 4).

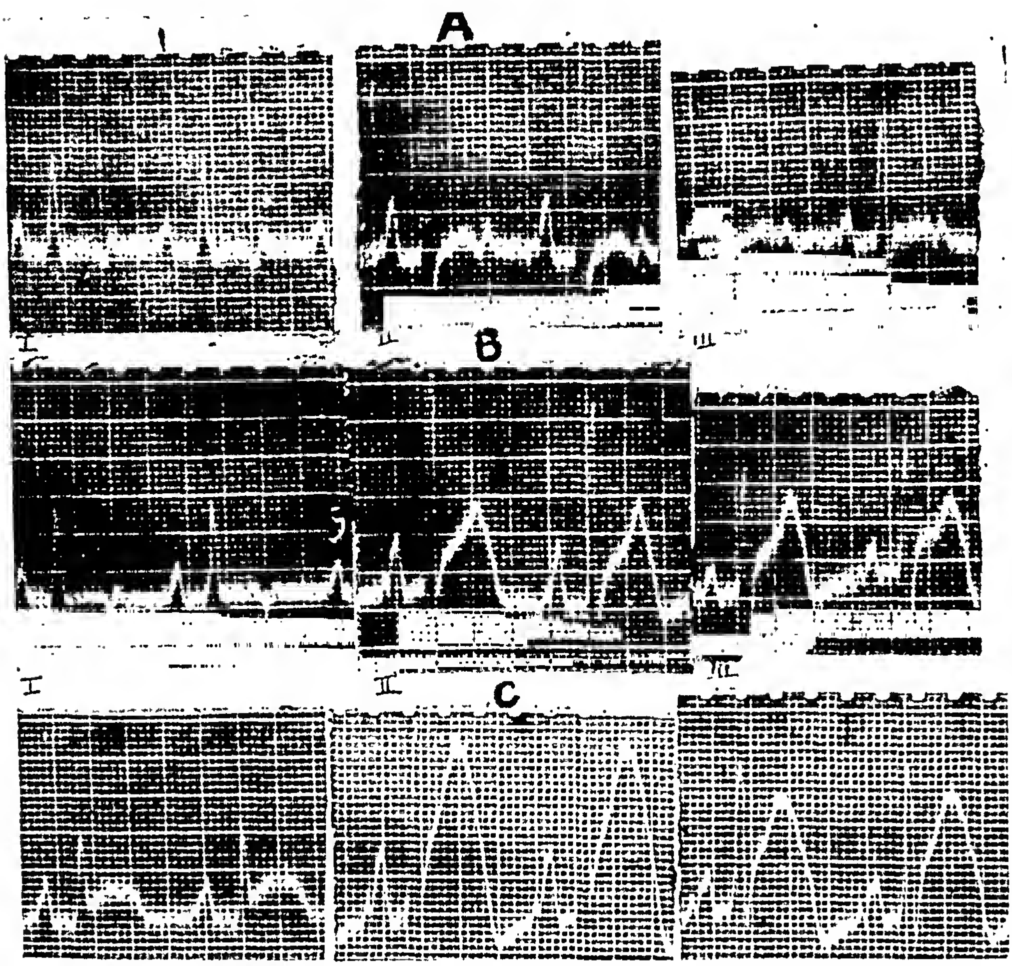

Fig. 4.—Electrocardiograms R.A.-L.A.; R.A.-L.L.; L.A.-L.L.; derivations I, II, III Time in fiftieth seconds. *A*, Normal. *B*, Ligature of the first branch and part of the second branch from the circumflex division of the left coronary artery. *C*, Ligature of a branch from the anterior division of the left coronary artery which also supplies this area.

Accelerator nerve stimulation had the same effect upon these electrocardiograms as upon the normal.[1, 6] Stimulation of the right nerve exaggerated the changes produced by closure of the right coronary artery and stimulation of the left nerve lessened them, causing the curve to approach the original form. Stimulation of the nerves in the presence of closure of left coronary vessels had the reverse effect, i.e., right nerve stimulation lessened the change and left nerve stimulation increased it.

Effects of Accelerator Nerve Section.—When the accelerator nerves were sectioned one hour before ligation, death occurred in a manner similar to that which occurred after ligature of the coronary sinus with the accelerator nerves sectioned, with dilatation and diminishing strength of contractions until standstill occurred. After this, ventricular fibrillation could very frequently be produced by faradization of the accelerator nerves. The ventricular fibrillation did not include the infarcted areas.* When the accelerator nerves were intact, death occurred by the onset of ventricular fibrillation. When the accelerator nerves were sectioned immediately before the ligature, death occurred by the onset of ventricular fibrillation whenever the time for the death to occur was short, otherwise the diastolic type of circulatory failure resulted. This was the single constant difference observed between the hearts in which the accelerator nerves were sectioned and

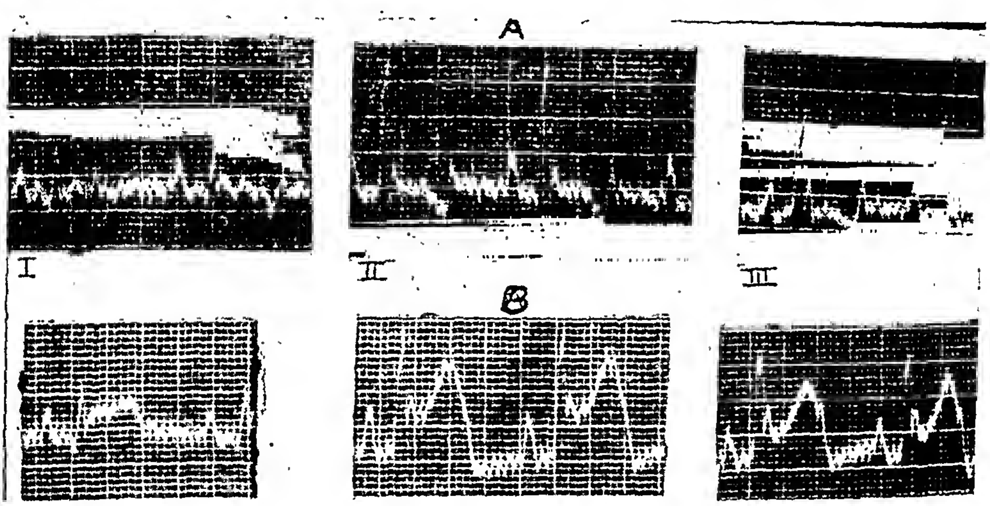

Fig. 5.—Electrocardiograms corresponding to derivations I, II, III. Time in fiftieth seconds. *A*, Normal. *B*, Ligature of second branch from the circumflex division of the left coronary artery (RT fusion).

those in which they were intact. No differences were observed in the time for the death to occur, in the resistance of the heart to the amount of the coronary arterial supply ligated, in the alterations in the rate or rhythm following the ligation, or in the amount of irritative phenomena (premature contraction or tachycardia) which appeared. It has already been mentioned that Danielopolu and Marcu[5] have observed significant changes to follow accelerator nerve section in the presence of coronary obstruction.

The Vagus.—There was no relation between the effect of maximum stimulation of the right vagus nerve and the amount of arterial ligature required to induce circulatory failure. There was a constant tendency, however, for the number of premature contractions which appeared after the ligation to be less numerous when the response to

*This has been described by Garrey[7], Lewis[2], Gold[8] and others.

vagus stimulation was marked. In order to test this further, the effect of prolonged vagus stimulation was tried in 8 other dogs, using faradic stimulation of the right vagus nerve in 4 and pilocarpine in large doses in the remainder, and it was found that the number of premature contractions was greatly diminished when compared to the number which followed coronary artery ligature under the same conditions without vagus stimulation, since in 6 of these animals very few premature contractions occurred, and in the other 2, although many appeared, the effect, when compared to the effect of ligature in hearts which presented a similar vagus reaction (very short stoppage time and a rapid rate of escape) also showed diminution in the number of premature contractions occurring.

SUMMARY AND CONCLUSIONS

1. The changes which follow closure of coronary vessels (arterial or venous) in the dog are not altered by section of the accelerator nerves except in the manner by which the death of the heart occurs. When the nerves are intact, death occurs by the onset of ventricular fibrillation and when they have been sectioned for one hour previously, death occurs by dilatation and diastole.

2. A diminished blood supply to the S-A node is suggested as the cause of nonrespiratory sinus arrhythmia and sinus block.

3. The electrocardiographic form of the premature beats which appear after closure of coronary arteries tends to follow the anatomical distribution of these vessels, since the closure of the left coronary arteries causes the appearance of premature beats, left ventricular in form, and the closure of the right coronary artery premature beats—right ventricular in form.

4. Closure of the right coronary artery causes negativity of the T-wave and the appearance of the ST fusion and the closure of left coronary vessels causes positivity of the T-wave and also the appearance of the RT fusion when the posterosuperior portion of the cardiac apex is thrown out of function.

5. Strong vagus nerve stimulation causes diminution in the number of premature contractions which occur as a result of coronary ligature.

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ABNORMALLY LONG PAPILLARY MUSCLES OF THE HUMAN HEART*

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ORDINARILY the papillary muscle of the human heart is attached to the valve leaflet by a number of fibrous chordae tendineae which are almost as long as, or even longer than, the muscle. Occasionally, however, macroscopic muscle bands extend upward into these cords and may even traverse their whole length, or more rarely, the papillary muscle itself may replace several chordae tendineae and be attached directly to the valve.

In the literature I have been able to find only two references to such anomalies, although they must certainly occur in the experience of every pathologist whose material from necropsies is abundant. In 1896 Przewoski described four cases. In three cases the tip of the normal papillary muscle in the left ventricle was prolonged into a thin extension which took the place of a cord. This form of the anomaly he did not consider altogether rare. He pronounced his fourth case to be more unusual; in this, a large anterior papillary muscle sent out a large muscular extension which entirely replaced several chordae tendineae and was inserted into the ventricular surface of the mitral valve up to the fibrous ring. Przewoski laid down the criterion that only the papillary muscles whose tip extended up to the valve should be considered abnormally long.

In 1910 Orsós-Pécs described twelve cases of anomalies of this type and mentioned another. In four of the described cases a cylindrical muscular beam from the anterior papillary muscle was inserted into the posterior leaflet of the tricuspid valve up to the attachment of the cusp. The lamella of insertion was relatively large. In the other eight cases muscular beams from the anterior papillary muscle of the left ventricle were inserted in the ventricular surface of the anterior leaflet of the mitral valve. When the muscle bundle was inserted into the middle of the valve leaflet, the plate of insertion was symmetric and triangular. When the bundle originated from the right side of the anterior papillary muscle, it fused with the corresponding part of the anterior cusp with a spade-shaped lamella of insertion which turned laterally and eventually connected with the ventricular wall. Orsós-Pécs explained the fact that the lamella of insertion of these bundles in the right ventricle always ended at the attached edge of the valve on the basis that the venous orifice of the right ventricle

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is bounded entirely by muscle, while in the left venous orifice the muscle over the anterior valvular cusp is missing. One of his patients was the son of another patient reported, a circumstance which argued that the anlage might be hereditary. In one case there was a calcified plaque at the point of insertion and in another on the auricular side of the point of insertion of the muscle bundle was a subendocardial tubercle. Orsós-Pécs thought these features could be explained by the stress of abnormal pull of the muscle.

I have found five cases of anomalies of this type. These occurred in about 550 necropsies, an incidence of 0.91 per cent.

Fig. 1.—(Case 1) Left anterior papillary muscle is inserted directly into the anterior cusp of the mitral valve just beneath the noncoronary cusp of the aortic valve.

REPORT OF CASES

Case 1.—The subject was a man, aged sixty years, who died from uremia following an acute exacerbation of chronic pyelonephritis. The systolic blood pressure was 220 mm. and the diastolic, 110 mm. The heart weighed 476 gm. (body weight, 61.4 kg., or 135 pounds). There was coronary sclerosis graded 2. With the exception of moderate hypertrophy, moderate coronary sclerosis and the anomaly, the heart appeared normal. The anterior papillary muscle of the left ventricle was 5.0 cm. long on its free inner surface and 2.5 cm. long on its mural surface (Fig. 1). It was 1.6 cm. broad at its base, which was formed by several fused trabeculae

carneae. From its base it tapered gradually upward into the ventricular surface of the anterior leaflet of the mitral valve with which it fused, extending in the valve to within 0.3 cm. of the line of attachment of the cusp to the membranous septum beneath the noncoronary cusp of the aortic valve. At its upper extremity it was 0.5 cm. broad and quite flat. From the posterior and lateral aspects of the papillary muscle the usual chordae tendinae were given off and were attached to the valve leaflets in the usual manner. One of the chordae tendineae was rather thick in its upper portion, but there was no evidence of preexisting endocarditis unless this thickened strand might be so considered. The posterior papillary bundles were of the usual form. The functional capability of the mitral valve was apparently normal.

Fig. 2.—(Case 2) The large left anterior papillary muscle comes to a point at the margin of the anterior cusp of the mitral valve. The apex, *a* is attached directly to the valve and short chordae tendineae are given off laterally from the muscle bundle.

Case 2.—The subject was a woman, aged forty-nine years, who died of cardiac decompensation following hypertension. The heart weighed 744 gm. (body weight, 73 kg., or 160 pounds). The left ventricle was considerably hypertrophied and dilated and the right ventricle was moderately hypertrophied and much dilated. The large anterior papillary muscle of the left ventricle was formed mainly by fusion of three trabeculae carneae, the middle muscular projection being the largest (Fig. 2). Above and on the right side the fused bundles came to a blunt point, 0.2 cm. broad, which was inserted into the free edge of the anterior leaflet of the mitral valve near its extreme right end, but the muscle did not penetrate far into the leaflet nor connect with the vetricular muscle. The insertion was more tendinous than muscular. Chordae tendinae, which were shorter than usual, arose from the sides of the papillary muscle and were inserted into the valve leaflets normally.

In this case the muscular attachment of the papillary muscle held the right end of the anterior leaflet in a rather fixed position, so that regurgitation would perhaps have been more marked if the mitral ring had become dilated.

Case 3.—The subject was a man, aged twenty-nine years, who died of electric shock. The heart appeared normal except for a few subepicardial petechiae. The left anterior papillary muscle consisted of one large, cone-shaped bundle with two smaller ones on the left and an anomalous bundle above and on the right (Fig. 3). The latter was connected with the main papillary muscle by narrow cords of muscle and with trabeculae carneae medial to it. It tapered as it ascended and was inserted into the ventricular surface of the anterior cusp of the mitral valve into which it extended halfway to the membranous attachment of the cusp close to its right side. It then connected with the muscle of the wall of the ventricle. Near

Fig. 3.—(Case 3) Anomalous muscle bundle, *b*, associated with the left anterior papillary muscle is inserted into the anterior cusp of the mitral valve.

the valve it sent off a small cylindrical beam of muscle upward and to the right which also joined the muscle of the wall of the ventricle. The lamella of insertion of the anomalous bundle was 0.4 cm. wide.

Case 4.—The subject was a man, aged thirty-eight years, who died of pulmonary complications following gastroenterostomy for duodenal ulcer. The mitral valve showed acute vegetative endocarditis. A number of chordae tendineae of the posterior papillary muscle of the left ventricle contained cylindrical bands of muscle which extended as far as the insertion of the cords into the mitral leaflets (Fig. 4). The most lateral muscle bundle of the papillary muscle gave rise to a muscular beam, 0.2 cm. in diameter in the middle, which extended into the posterior cusp of the mitral valve, becoming thicker as it approached the valve. It contained some tendinous strands and at the upper extremity divided into two main muscular

beams and several small chordae tendineae. At about the middle it had a small muscular beam connecting it to one of the trabeculae carneae of the wall of the ventricle.

Case 5.—The subject was a boy, aged fourteen years, who died of suffocation due to inhalation of food into the bronchi. The heart was somewhat hypertrophied, weighing 271 gm. and both ventricles were considerably dilated. On the anterior wall of the right ventricle was the usual large papillary muscle, but instead of having the common attachment of chordae tendineae to the adjacent halves of the medial and anterior cusps of the tricuspid valve it passed directly up under the ventricular surface of the anterior cusp (Fig. 5). It gave off a few chordae

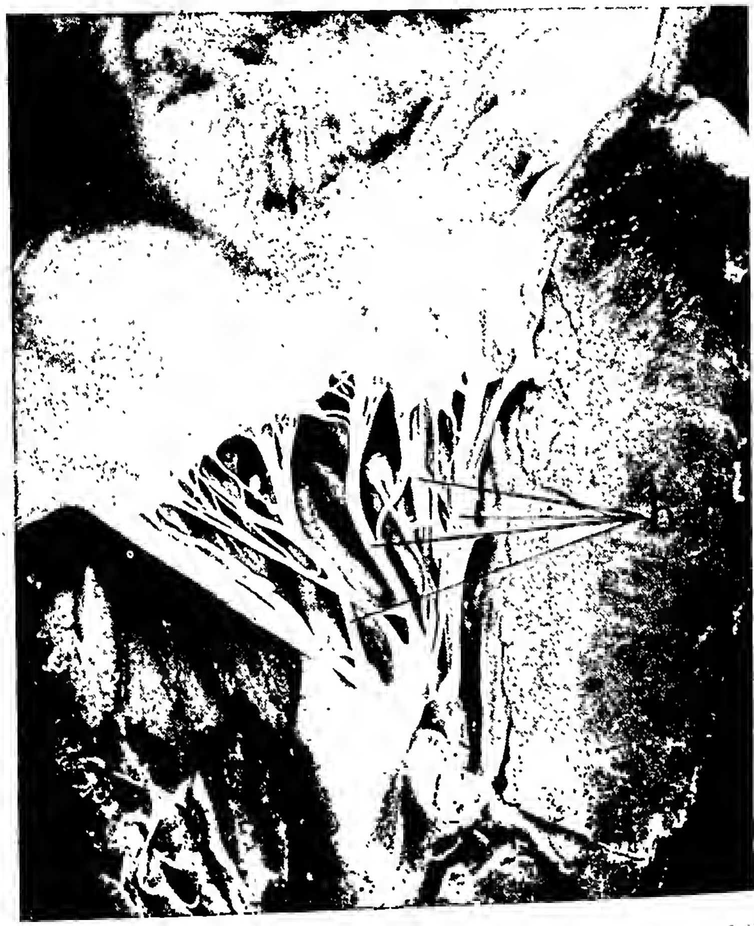

Fig. 4.—(Case 4) Muscle bundles, *b*, are in the chordae tendineae of the left posterior papillary muscle traversing the whole length and extending to the mitral cusps, especially the posterior.

tendineae and became a flat lamella, 0.7 cm. wide, which was inserted in a straight line into the fibrous cusp, 0.55 cm. from the attachment of the valve; several strands of muscle could be seen by transillumination of the cusp passing from this line of insertion to the muscle at the attached edge of the valve. The free portion of the papillary muscle was 2.7 cm. long. Just to the left side of this papillary muscle was a small one which had chordae tendineae attached to the adjacent edges of the medial and anterior cusps of the tricuspid valve but which also sent a narrow muscular lamella up under the valve to be inserted by a flat triangular enlargement into the cusp near its line of attachment; between this triangular lamella of insertion and the papillary muscle proper was a small fibrous area in which muscle

was not visible macroscopically. On the right side of the main papillary muscle was another small papillary muscle, the chordae tendineae of which were attached to the adjacent edges of the medial and posterior cusps of the valve. Several very small papillary muscles gave rise to chordae tendineae which were attached to the posterior cusp.

COMMENT

This type of anomaly is undoubtedly congenital. Early in the development of the atrio-ventricular valves muscular tissue from the myocardium invades the endocardial tissue of the cusps and replaces it. The muscular tissue of the cusps becomes closely blended with the

Fig. 5.—(Case 5) The papillary muscles of the right ventricle (retouched) are cut loose and turned upward to expose their ventricular surfaces. The large papillary muscle, *b*, is inserted into the anterior cusp of the tricuspid valve. The smaller papillary muscle, *b'*, also has a muscular lamella of insertion.

subjacent musculature of the walls of the ventricles. This stage in the development of the cusps is soon followed by replacement of the muscular tissue by collagenous connective tissue, the process evidently taking place mainly from above downward. The subjacent trabeculate musculature also is replaced by collagenous connective tissue. The fibrous cords so developed are the chordae tendineae. Muscular tissue persists at the parietal ends of the cords and forms the papillary muscles. In cases such as those just described the replacement by collagenous connective tissue ceases too soon or is imperfect, and muscular tissue is left in place of chordae tendineae.

The only other explanation would be that localized endocarditis had produced thickening and retraction of the chordae tendineae, causing the cusp of the valve and the papillary muscle to be drawn together. All the facts, however, are opposed to this conception and point rather to the developmental origin of the condition.

The instances of this anomaly previously reported and those described in this paper have not appeared to possess any clinical significance. In Case 2 of this series it seemed that the condition might have increased the insufficiency of a dilated mitral ring had such been present, but the mitral orifice was apparently not very incompetent.

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THE RELATION OF THE WEIGHT OF THE HEART TO THE WEIGHT OF THE BODY AND OF THE WEIGHT OF THE HEART TO AGE*

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WHAT is the normal weight of the human heart? What are the upper and lower limits of normal? Which weights should be considered normal and which abnormal? Just where is the line to be drawn between the normal and the abnormal? The literature is at variance on the subject of just what constitutes the normal or average weight of the human heart and it contains little, if any, information concerning the upper and lower limits of normal. It is necessary, therefore, to arrive at some conclusion regarding the foregoing questions before it can be said that certain diseases do or do not cause the heart to enlarge. In this study I have attempted to learn something definite with regard to the weight of the normal heart.

MATERIAL

Ideal material for such study obviously cannot be obtained since the heart after death is not absolutely comparable to the normal heart during life. The nearest approach to ideal material would be a heart obtained from a person dying suddenly from accidental causes who had been in perfect health as revealed by recent general examination. It would, of course, be impossible to obtain enough material of this type to give any conclusive results. The most ideal available material is that of hearts obtained from patients who have died from diseases that have not affected the size or weight of this organ.

The most satisfactory material for this study was obtained from accident cases with and without operation. Other satisfactory material came from cases of acute and chronic appendicitis, hernias, and gynecological cases in which the patient had died from pulmonary embolism, pneumonia, or shock following operation. A large percentage of cases were carcinoma of the stomach, breast, colon and sigmoid, tumor of the brain, and peritônitis following operation for lesions of the gall bladder, bowel, prostate and kidneys.

The age, sex, height, weight of the body, weight of the heart, anatomical diagnosis, gross and microscopic diagnosis of the condition of the heart, the blood pressure readings, and the degree of existent arte-

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riosclerosis were obtained from necropsy records and clinical histories in The Mayo Clinic in 1000 cases.

Cases Excluded.—If specimens are to be used only from cases in which the disease did not affect the size or weight of the heart, it is apparent that a large percentage of cases examined in any gross series will be rejected.

The records of all diseases known or supposed to affect the weight of the heart were excluded. All cases of lesions of the heart were discarded, as well as those in which a clinical diagnosis had been made of cardiac disease, that is, pericarditis, endocarditis, and diseases of the myocardium, such as fatty changes, myocarditis, arteriosclerosis, hypertrophy, and dilatation. All cases of systemic diseases that are commonly believed to affect the size and weight of the heart were rejected. Among these were syphilis, pernicious anemia, arteriosclerosis exceeding Grade 1, chronic nephritis, hypertension,* exophthalmic goiter and adenomatous goiter with hyperthyroidism, and longstanding bronchial asthma. All cases presenting signs or symptoms of cardiac decompensation were excluded, as were those in which the heart was enlarged without demonstrable cause. By this method of selection, the number of acceptable cases was greatly reduced as evidenced by the fact that 6000 protocols were examined in order to obtain the 1000 used in this series.

Weight of the Body.—Practically all of the patients had been weighed during their examination at the clinic and had also stated their normal weight. If there was a marked difference between the weight at entrance and the normal weight, the latter was used. This difference was especially noteworthy in cases of malignant tumors in some of which from 20 to 40 pounds had been lost. An objection might be made to this material. If the normal weight of the body is accepted the weight of the heart will be relatively small, since it may have lost a little of its fat. If, however, the entrance weight is accepted the error would be much greater. In like manner, the normal weight given by the patient generally includes the clothing, whereas the entrance weight includes only a sheet and cape, weighing approximately 0.68 kg. (1.5 pounds). It is not likely that these slight inherent errors in technic have influenced the results appreciably.

LITERATURE

Boyd[4] (1861) studied this subject from cadavers at Morylebone Infirmary and from an insane asylum at Sommerset. He apparently did not select his material.

Thoma,[16] Müller,[12] Vierordt,[17] and Kress[10] made extensive investigations. Vierordt and Kress, however, did not record weights. Thoma's figures are based on the average weight of the heart from

*Systolic blood pressure readings exceeding 145 for any age.

published data combined with his own study of the average weight of the body for corresponding ages. Müller weighed both the heart and the body but, so far as can be determined, did not consider the clinical data. A considerable percentage of the cases in many of his studies were of extremely emaciated infants. He studied the relation of the weight of the heart, and of the muscle of the heart, to the weight of the heart as a whole and to the weight of the body, and also its relation to height and age (Table 1).

From their results it is apparent that there must be a correlation between the weight of the body and that of the heart, probably due to the "need of a given mass of heart muscle to pump the blood to a given mass of tissue."

Bardeen[2] concluded that 0.55 per cent of the body weight approximated closely the normal relative proportion of the weight of the heart in males at all ages except at birth and immediately thereafter (Table 1). In females, the relative proportion is about 0.53 per cent of the body weight.

From Müller's observations (Table 1) the weight of the heart is approximately 0.50 to 0.75 per cent of the weight of the body in persons of normal height and weight, being slightly higher in males and lower in females; higher in thin persons and lower in obese persons. Müller concluded that there is "an increase in the relative weight of the heart with age, *irrespective of the size of the body*."

Gray[5] has stated that the heart continues to increase in weight and size up to an advanced period of life and that this increase is more marked in men than in women.

Müller found that the weight of the left ventricle is approximately twice that of the right ventricle. The ventricles weigh approximately four times as much as the auricles, and the weight of the valves is 2 per cent of the total weight of the heart. The fat content increases with age. In the newborn infant there is relatively little fat. He found in males that the relative weight of cardiac fat to body weight is 0.077 per cent in the range from two to fifty years with 0.057 per cent as the minimum. Below the second year, he found the percentage much less, and after fifty years it is considerably greater. He also estimated that the intrapericardial part of the great vessels of the heart is 0.005 per cent of the weight of the body. This is increased with age. The weight of the heart is 5.5 gm. per kilogram of body weight and its specific gravity is about 1.050.

Greenwood and Brown[6] concluded that there is a correlation between the weight of the heart and the weight of the body, and that the weight of the heart can be calculated from the weight of the body with an error of about 8 per cent. They found that by dividing the weight of the heart by the weight of the body, the heart is approximately 0.575 per cent of the body weight. There was a variation from

TABLE I

PROPORTIONAL WEIGHT OF THE HEART AT VARIOUS AGES AS REPORTED BY SEVERAL INVESTIGATORS

AGE	OBSERVER																				
	BOYD				THOMA	MÜLLER				VIERORDT				KRESS			
	MALE		FEMALE			MALE		FEMALE		MALE		FEMALE		MALE		FEMALE	
	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	ESTIMATE BASED ON VARIOUS DATA	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY
Birth	44	0.648	42	0.572	0.625	23	0.62	14	0.63	62	0.76	59	0.80	3	0.66	6	0.89
months																	
1	16	0.594	21	0.651		45	0.64	47	0.63	7	0.51	12	0.49	2	0.83		
2-3						50	0.58	52	0.61	30	0.48	33	0.38	6	0.68	7	0.65
4-6	15	0.605	24	0.716	0.444					28	0.38	26	0.36	8	0.67	11	0.64
7-9										29	0.40	18	0.29	7	0.64	9	0.65
10-11	46	0.516	40	0.628		34	0.60	32	0.60	6	0.41	6	0.44	6	0.54	5	0.67
years																	
1					0.412					15	0.46	18	0.42	4	0.59	7	0.58
2	34	0.736	32	0.711	0.422	34	0.62	42	0.62	45	0.47	52	0.53	12	0.60	4	0.60
3	27	0.662	29	0.716	0.417					31	0.52	37	0.50	10	0.58	7	0.61
4					0.40	16	0.58	19	0.59	32	0.53	18	0.55	10	0.64	8	0.61
5					0.382					24	0.51	30	0.55	8	0.54	7	0.60
6	27	0.676	20	0.592	0.383					7	0.48	17	0.56	7	0.65	7	0.64
7					0.392					18	0.47	6	0.48	7	0.61	5	0.64
8					0.402	15	0.62	18	0.56	3	0.44	11	0.58	5	0.80		
9					0.417					6	0.46	4	0.62	5	0.65	2	0.66
10					0.433					10	0.51	3	0.54	5	0.60	2	0.58
11					0.452					12	0.52	5	0.47	2	0.49	2	0.60
12					0.474					1	0.34	1	0.40				
13	21	0.634	17	0.706	0.481	9	0.60	10	0.55	8	0.50	2	0.46	2	0.63	3	0.54
14					0.490					8	0.58	8	0.50	4	0.61	1	0.60
15					0.500					9	0.48	11	0.65	5	0.62	35	0.52

TABLE I- CONT'D

AGE	OBSERVER																	
	BOYD				THOMA	MÜLLER				VIERORDT				KRESS				
	MALE		FEMALE			MALE		FEMALE		MALE		FEMALE		MALE		FEMALE		
	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	ESTIMATE BASED ON VARIOUS DATA	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	
16					0.481					11	0.51	10	0.63					
17					0.471					17	0.51	16	0.52					
18	18	0.699	15	0.762	0.474	23	0.55	13	0.50	20	0.46	25	0.49					
19					0.474					23	0.51	15	0.53					
20					0.476					15	0.51	30	0.48					
21					0.481					33	0.49	22	0.48					
22					0.483					27	0.50	21	0.48					
23					0.490					21	0.48	22	0.49					
24					0.495					30	0.46	22	0.49					
25-30	58	0.675	74	0.654	0.502	73	0.58	45	0.50	30	0.46	27	0.49					
	46	0.597	29	0.608														
31-40	118	0.720	87	0.682		70	0.56	59	0.52									
	59	0.600	49	0.470														
41-50	137	0.705	106	0.706		84	0.59	69	0.56									
	76	0.690	49	0.676														
51-60	119	0.719	106	0.764		87	0.62	61	0.59									
	42	0.637	39	0.710														
61-70	126	0.763	149	0.758		88	0.64	83	0.64									
	39	0.728	41	0.716														
71-80	100	0.774	150	0.786		64	0.64	61	0.67									
	21	0.693	20	0.612														
81-90	24	0.840	76	0.806		11	0.75	12	0.69									
	7	0.740	5	0.655														

the mean percentage of about 25 per cent in each direction, that is, from 0.45 per cent to 0.7 per cent of the weight of the body.

Boyd's figures show a higher percentage than do the others', ranging from 0.6 to 0.8 per cent instead of less than 0.6 per cent. He found very little differences between the percentages of males and females.

Scammon[15] concluded: "The heart weighs at birth from 20 to 25 gm. The weight of the heart at birth doubles in the first two years of life. The weight of the heart at birth triples in four years. The weight of the heart at birth increases sixfold at puberty. There is a rapid increase in heart weight during adolescence. The adult heart weighs ten to thirteen times that of the newborn. The relative heart weight of the newborn is distinctly greater than that of the adult. At birth the heart forms 0.65 to 0.80 per cent of the body weight. During the second year the relative heart weight is about 0.5 per cent of the body weight and this relation obtains, with individual variation, through the remainder of childhood and maturity."

METHOD OF STUDY AND FINDINGS

The heart consists of (1) muscles; (2) connective tissue of the valves and supporting structures; (3) intrinsic blood vessels of the heart and the great vessels near their attachments to the heart, and (4) fat beneath the pericardium and elsewhere in the heart. The length and size of large vessels left attached to the heart will affect the weight to some degree. In my study the hearts were opened and washed before being weighed. The specimens were divided according to age and then subdivided according to sex (Table II).

Accurate conclusions cannot be drawn from the age groups from five to seven years and from eighteen to twenty-one years, since there were only fourteen and twenty-nine cases respectively in these groups. In fact, all the results in the age groups up to twenty-one years are not wholly reliable or accurate because they are affected by the growth curves. The age group from forty-one to fifty years was the only group in which the percentage of body weight was higher in the females than in the males.

The highest percentages of body weight occurred in the group of premature births, 0.98 per cent for males and 0.91 per cent for females. In the group from birth to one year the percentages were 0.62 per cent for males and 0.55 per cent for females. The percentage in the remaining males ranged from 0.35 to 0.46 per cent. The adult male age groups showed a range in percentage from 0.42 to 0.46. In the female groups of all ages the percentage ranged from 0.37 to 0.91. The percentage ranged from 0.38 to 0.46 for the adult females.

TABLE II

AGE, YEARS	TOTAL NUMBER OF CASES	MALE	FEMALE	HEART WEIGHT GM.			BODY WEIGHT						HEIGHT CM.			PERCENTAGE OF BODY WEIGHT
							MINIMUM		MAXIMUM		AVERAGE					
				MINIMUM	MAXIMUM	AVERAGE	POUNDS	KILOGRAMS	POUNDS	KILOGRAMS	POUNDS	KILOGRAMS	MINIMUM	MAXIMUM	AVERAGE	
Premature	28	15		4	86	20.4	2	0.9	12	5.4	4.6	2.0	33	62	43.4	0.98
			13	8	51	22.0	3	1.3	9	4.0	5.3	2.4	32	50	45.0	0.91
Birth to 1 year inclusive	34	17		15	95	45.0	6	2.7	35	15.0	16.0	7.2	44	98	66.0	0.62
			17	10	83	35.0	4	1.8	30	13.0	14.0	6.3	42	86	63.0	0.55
2-4	27	17		45	98	69.0	16	7.2	60	27.0	35.0	15.9	44	107	86.5	0.43
			10	27	83	55.5	20	9.0	50	22.0	33.0	15.0	78	96	88.0	0.37
5-7	14	8		60	113	87.7	40	18.0	65	29.0	56.0	25.0	107	119	112.5	0.35
			6	60	144	94.0	33	15.0	90	40.0	56.0	25.0	109	131	117.0	0.37
8-12	17	13		81	186	149.0	40	18.0	110	50.0	73.5	33.0	105	153	135.0	0.44
			4	93	150	120.0	50	22.0	80	36.0	63.0	24.0	120	146	132.0	0.419
13-17	26	18		151	320	225.0	80	36.0	150	68.0	115.0	52.0	144	177	161.0	0.43
			8	120	243	180.0	50	22.0	150	68.0	103.0	46.0	151	171	160.0	0.38
18-21	29	19		225	354	308.0	110	50.0	170	77.0	149.0	67.0	159	189	174.0	0.42
			10	202	284	245.0	100	45.0	175	79.0	127.0	57.0	155	165	160.0	0.42
22-30	90	56		155	388	282.0	100	45.0	180	81.0	138.0	62.0	160	185	171.0	0.44
			34	155	310	223.0	85	38.0	195	88.0	126.0	57.0	130	172	158.0	0.38
31-40	179	98		190	380	290.0	90	40.0	190	86.0	146.0	66.0	144	195	173.0	0.44
			81	110	365	243.0	90	40.0	200	90.0	134.0	60.0	152	176	163.0	0.40
41-50	221	138		196	400	302.0	100	45.0	208	94.0	153.0	69.0	154	186	165.0	0.43
			83	148	350	270.0	95	43.0	210	95.0	127.0	57.0	145	186	162.0	0.46
51-60	222	134		140	397	294.0	110	50.0	250	113.0	148.0	67.0	159	187	171.0	0.44
			88	160	367	263.0	80	36.0	220	100.0	143.0	65.0	130	181	162.0	0.40
61-70	100	76		210	386	289.0	100	45.0	200	90.0	138.0	62.0	162	182	171.0	0.46
			24	171	305	259.0	100	45.0	221	100.0	134.0	60.0	146	172	162.0	0.42
71-80	13	13		137	375	292.0	120	54.0	170	76.0	141.0	64.0	166	185	174.0	0.45

One is impressed by the close ratios of each group. The total average of the weight of the heart of all the adult male groups is 0.43 per cent of the weight of the body and of the female is 0.40 per cent. It is possible that the percentages are slightly too high since the body weights were apparently slightly below normal (Table I).

Boyd's percentages ranged from 0.59 to 0.84 for males and 0.51 to 0.80 for females.

Thoma's average percentage of the weight of the heart varied from 0.38 to 0.49.

Müller's percentages had a scope of 0.55 to 0.75 for males and 0.50 to 0.69 for females.

Gray stated the relative weight of the heart for males as 1:160 or 0.62 per cent, and as 1:150 or 0.66 per cent for females (Table III).

Piersol found the relative weight of the heart for males to be as 1:169 or 0.59 per cent and for females as 1:162 or 0.61 per cent.

Gray and Piersol both give a relatively higher weight of the heart for the females. In only two of the age groups of my series did a relatively higher percentage weight for the females occur. In nine age groups the percentage of the male was higher and in one group the percentage for the males and females was the same.

Müller stated further: "There is an increase in the relative weight of the heart with age, irrespective of the size of the body." Gray stated: "The heart continues to increase in weight and size up to an advanced period of life" and, "This increase is more marked in males than in females." He then paradoxically stated that the weight of the heart of the female is relatively higher. Other investigators agree with Gray and Müller that the weight of the heart increases with age.

During the War, Aschoff studied the weight of the hearts of 685 soldiers (Table IV); the average weight was 321 gm.

Cruveilhier found the average weight of the heart for males to be 240 gm. and for females 210 gm.

The conclusions drawn from my study do not agree with the statement: "The weight of the heart increases with age, irrespective of weight." Probably the reason that other observers obtained a higher percentage of weight of the heart and concluded that the heart increased with age irrespective of the weight of the body was owing to the fact that they did not exclude hypertensive hearts.

The total average for all adult age groups was 294 gm. for males and 250 gm. for females. The smallest heart for the males in the adult age groups was 155 gm. and the largest was 400 gm. Only one heart weighed 400 gm. There was nothing in the history of the case to justify its exclusion. The subject was an unusually well-developed man weighing 93.6 kg. (208 pounds). The smallest heart of a female in the adult age group was 110 gm., the largest was 367 gm.

TABLE III

RELATIVE WEIGHT OF THE HEART BY VARIOUS AUTHORS

AUTHOR	AVERAGE WEIGHT OF HEART, GM.		PER CENT OF WEIGHT OF BODY	
	MALE	FEMALE		
Gray	280-340	230-280		
Davis	280	250		
Morris	321	230-250	1:205	
Piersol	266-346	230-340	Male 1:169 or 0.59	Female 1:162 or 0.61
Cunningham	310	255	Birth 1:130 0.76	Adult 1:205 0.5+

TABLE IV

WEIGHT OF HEART AMONG SOLDIERS (ASCHOFF)

AGE, YEARS	HEIGHT, METERS	WEIGHT OF HEART, GM.
18-19	1.65	300 (19)*
20-24	1.70	299 (133)
25-29	1.72	327 (102)
30-34	1.72	328 (85)
35-39	1.75	319 (65)
40-44	1.69	355 (45)
45-50	1.66	319 (19)

*Number in parenthesis denotes number of 468 cases in each group.

The smallest weight of the body in the adult male group was 40.5 kg. (90 pounds) and the largest was 112.5 kg. (250 pounds). The average was 64.8 kg. (144 pounds). The smallest weight of the body in the adult female group was 38.3 kg. (85 pounds) and the largest 99.5 kg. (221 pounds). The average was 59 kg. (131 pounds). There were relatively few of the extremely small or large weights.

In this series the weight of the heart did not increase with age. The largest male hearts were in the age groups eighteen to twenty-one years, but in each group the weight was quite constant. The average weight of the heart varied from 282 to 308 gm. In the last group there were only thirteen cases, but these thirteen cases conformed with the other age groups. In Fig. 1 where the weight of the heart over weight of the body is plotted against the age groups, there is a sudden fall followed by virtually a straight line. Only twice does the female line cross the male and that is in the five to seven year and in the forty-one to fifty year age groups. In Fig. 2 the weight of the heart is used as the ordinate and the age group as abscissa. The curve from birth up to the adult period simulates Seammon's growth curve and from the beginning of the adult period on tends to follow a straight line. In Fig. 3 the heart weight in grams is plotted against the body height in centimeters. One can reasonably conclude from this curve that the height affects the heart weight only as the height affects the body weight.

In 1914 Allen Hazen ruled some paper with a horizontal scale, so divided that the curve of probability would plot a straight line and hence any series of observations which varied in accordance with the law of arithmetic probability would also plot as straight lines. The

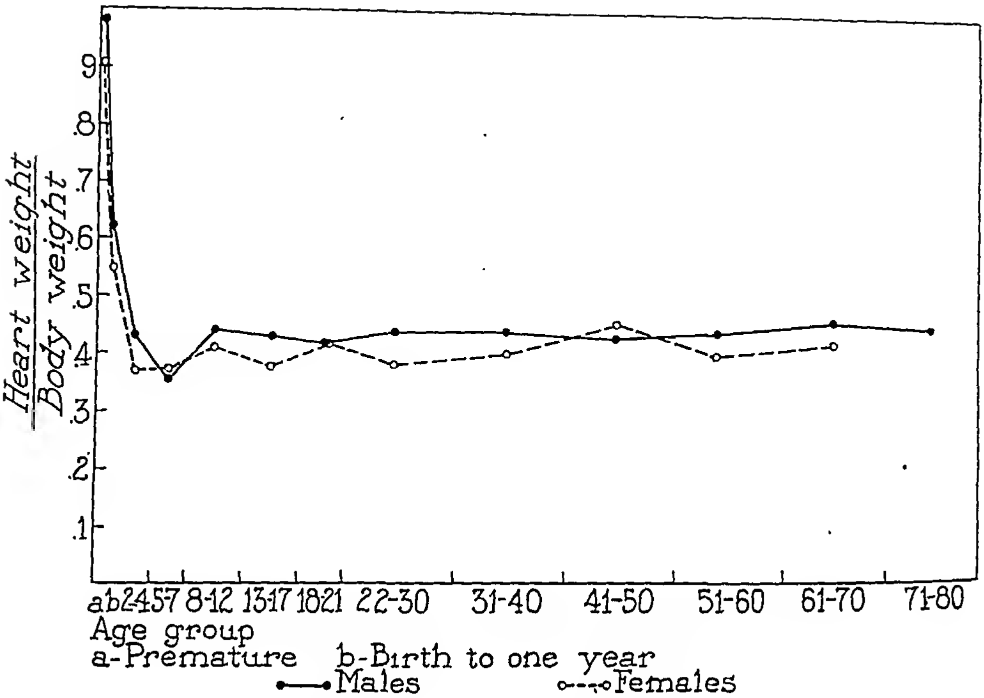

Fig. 1.—Ratio of weight of heart to weight of body for various age groups.

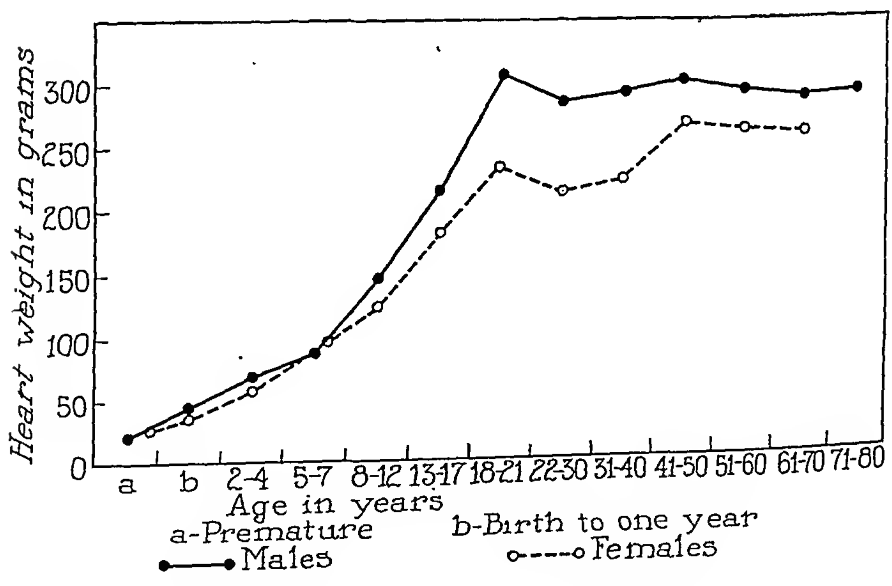

Fig. 2.—Weight of heart for various age groups.

converse is also true, that is, any series of observations plotted on this paper that plot a straight line will vary in accordance with the law of arithmetic probability.

The different age groups were taken, male and female, and plotted on probability paper and all plotted fairly straight lines (Figs. 4 and

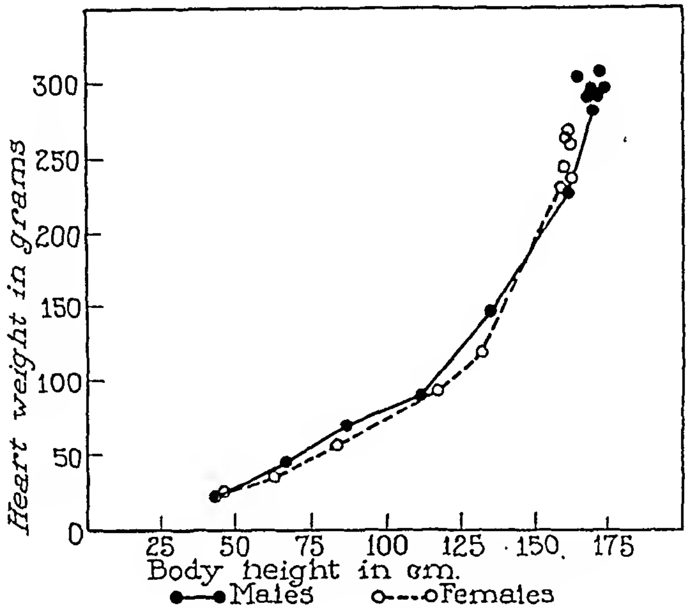

Fig. 3.—Relation of weight of heart to height.

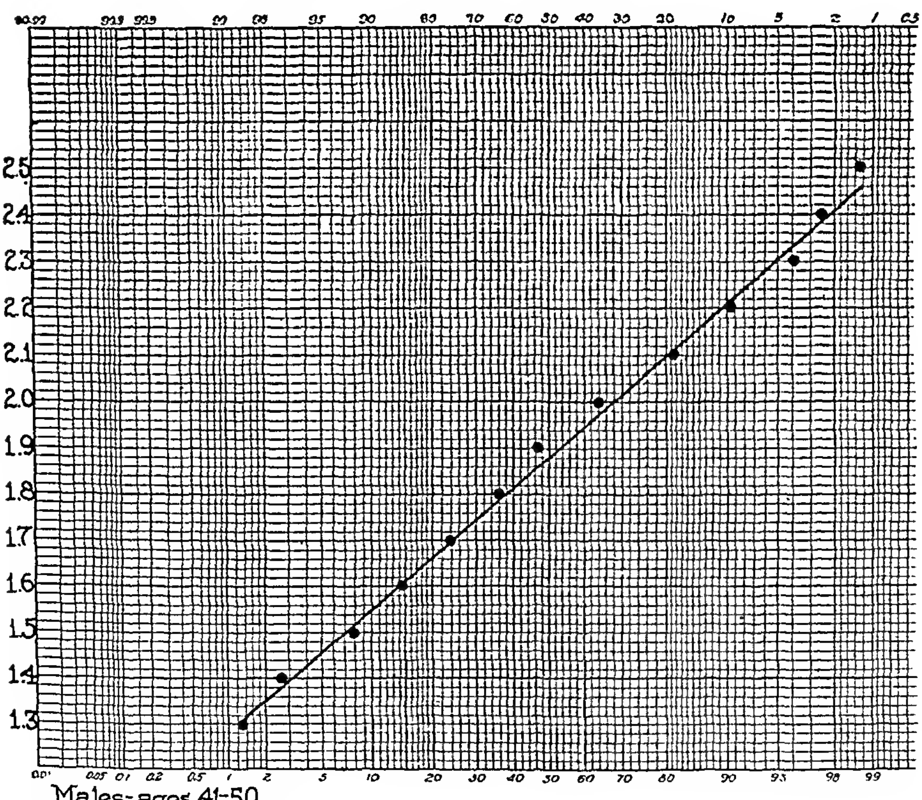

Fig. 4.—Percentage of weight of heart to weight of body plotted against percentage of cases for males aged from forty-one to fifty.

5). For the abscissas the percentage of the number of cases was used and the percentages of heart weights to body weights as the

ordinates. In Fig. 4 (males aged from forty-one to fifty) there were 1.2 per cent of that group in which the ratio of the weight of the heart to the weight of the body was 1.3 or less. There were 2.3 per cent in which the ratio was 1.4 or less and 10 per cent in which the ratio was 1.5 or less. In 15 per cent the ratio was 1.6 or less, in 25 per cent 1.7 or less, in 37 per cent 1.8 or less, in 48 per cent 1.9 or less, in 66 per cent 2.0 or less, in 82 per cent 2.1 or less, in 91 per cent 2.2 or less, in 97 per cent 2.3 or less, in 98.5 per cent 2.4 or less, and in 99.5 per cent 2.5 or less.

Fig. 6 represents the curves with low and high weights of the body. The curve for low weights is more vertical than the one for

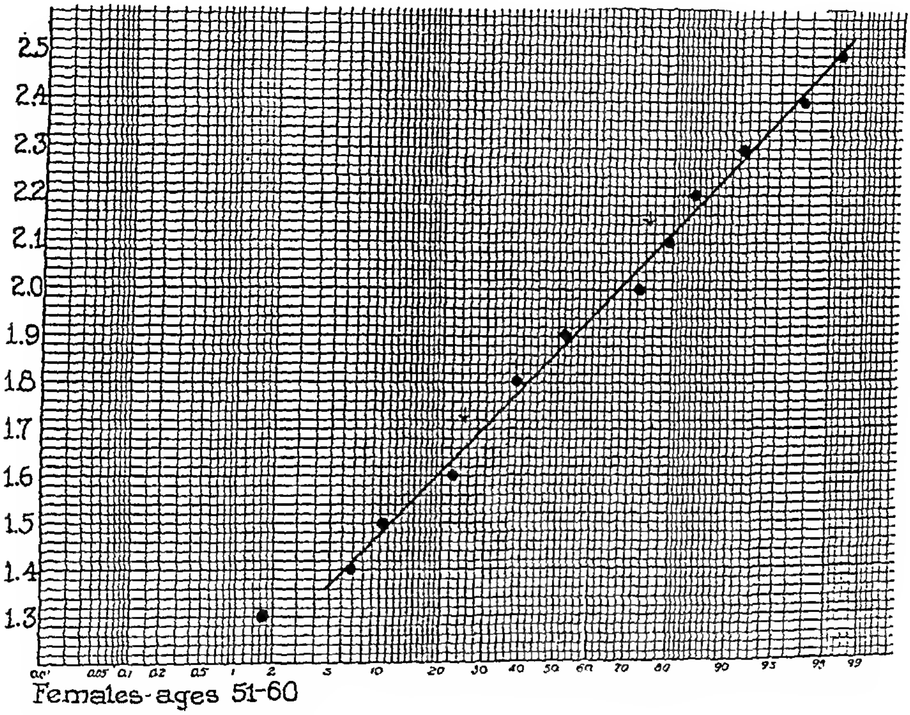

Fig. 5.—Percentage of weight of heart to weight of body plotted against percentage of cases for females aged from fifty-one to sixty.

high weights. The average ratio for the high weights is lower than that for the average weights. The average ratio for low weights is 1.9 and for the high it is 1.6.

Variation.—When many different measurements of a certain quantity have been made, it is common to generalize them by computing the averages, that is, the numerical mean. This often fails to give a complete visualization of the individual measurements in a series. Two groups of items of very different magnitude may yield the same average; for example, the average of 5, 6, 5, 8 and 6 is 6, and likewise the average for 1, 2, 1, 3 and 23 is 6.

In my series of cases relatively few very low or very high weights

published data combined with his own study of the average weight of the body for corresponding ages. Müller weighed both the heart and the body but, so far as can be determined, did not consider the clinical data. A considerable percentage of the cases in many of his studies were of extremely emaciated infants. He studied the relation of the weight of the heart, and of the muscle of the heart, to the weight of the heart as a whole and to the weight of the body, and also its relation to height and age (Table I).

From their results it is apparent that there must be a correlation between the weight of the body and that of the heart, probably due to the "need of a given mass of heart muscle to pump the blood to a given mass of tissue."

Bardeen[2] concluded that 0.55 per cent of the body weight approximated closely the normal relative proportion of the weight of the heart in males at all ages except at birth and immediately thereafter (Table I). In females, the relative proportion is about 0.53 per cent of the body weight.

From Müller's observations (Table I) the weight of the heart is approximately 0.50 to 0.75 per cent of the weight of the body in persons of normal height and weight, being slightly higher in males and lower in females; higher in thin persons and lower in obese persons. Müller concluded that there is "an increase in the relative weight of the heart with age, *irrespective of the size of the body.*"

Gray[8] has stated that the heart continues to increase in weight and size up to an advanced period of life and that this increase is more marked in men than in women.

Müller found that the weight of the left ventricle is approximately twice that of the right ventricle. The ventricles weigh approximately four times as much as the auricles, and the weight of the valves is 2 per cent of the total weight of the heart. The fat content increases with age. In the newborn infant there is relatively little fat. He found in males that the relative weight of cardiac fat to body weight is 0.077 per cent in the range from two to fifty years with 0.057 per cent as the minimum. Below the second year, he found the percentage much less, and after fifty years it is considerably greater. He also estimated that the intrapericardial part of the great vessels of the heart is 0.005 per cent of the weight of the body. This is increased with age. The weight of the heart is 5.5 gm. per kilogram of body weight and its specific gravity is about 1.050.

Greenwood and Brown[9] concluded that there is a correlation between the weight of the heart and the weight of the body, and that the weight of the heart can be calculated from the weight of the body with an error of about 8 per cent. They found that by dividing the weight of the heart by the weight of the body, the heart is approximately 0.575 per cent of the body weight. There was a variation from

TABLE V

NORMAL WEIGHT OF THE HEART: MALES

BODY WEIGHT POUNDS	BODY WEIGHT KILOGRAMS	MINIMUM GM.	AVERAGE GM.	MAXIMUM GM.
105	47	165	205	241
110	50	173	215	253
115	52	181	225	264
120	54	190	235	276
125	56	198	245	287
130	58	206	255	299
135	60	213	265	310
140	63	221	274	322
145	65	229	284	333
150	68	237	294	345
155	70	245	304	356
160	72	253	313	368
165	74	261	323	370
170	77	268	333	371
175	79	280	343	372
180	81	288	353	373
185	83	296	363	382
190	86	304	373	392
195	88	312	382	402
200	90	320	392	412

TABLE VI

NORMAL WEIGHT OF THE HEART: FEMALES

BODY WEIGHT POUNDS	BODY WEIGHT KILOGRAMS	MINIMUM GM.	AVERAGE GM.	MAXIMUM GM.
90	40	135	162	193
95	43	143	171	204
100	45	150	180	215
105	47	158	189	226
110	50	165	198	237
115	52	172	207	248
120	54	180	215	259
125	56	188	225	268
130	58	195	234	277
135	60	203	244	286
140	63	211	253	295
145	65	219	262	304
150	68	225	272	313
155	70	233	282	322
160	72	240	288	330
165	74	247	297	337
170	77	255	306	343
175	79	283	315	350
180	81	301	324	356
185	83	309	333	361
190	86	317	342	366
195	88	325	351	371

CONCLUSIONS

1. The average weight of the adult male heart is 294 gm.; the average weight of the adult female heart is 250 gm.

2. There is a definite correlation between weight of the heart and weight of the body. The ratio is 0.43 per cent for males, and 0.40

per cent for females. The ratio is slightly higher in thin persons and lower in obese persons. This coefficient is not so accurate for body weights of less than 45 kg. (100 pounds) and more than 94.5 kg. (210 pounds).

3. The weight of the heart may be calculated from the weight of the body with an error varying from 8 to 10 per cent.

4. The weight of the heart does not increase with age, irrespective of the weight of the body. The weight of the heart increases with increase in weight of the body.

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OBSERVATIONS ON THE MORTALITY OF HEART DISEASE IN NEW YORK STATE*

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THESE remarks are based upon information gathered by and for the Committee to Study Heart Disease of the New York State Medical Society.†

The importance of the mortality of heart disease in the State mortality statistics is shown by the comparison of its yearly rate per 100,000 with six other principal causes of death. The term heart disease includes the four numbers of the International List. In the graphic comparison (Fig. 1) there are two striking features: first, the curve of rates for heart disease is well above all the other rate curves and, second, since 1917 (Table I) the rate has risen progressively from 251 to 303 in 1926. Compared with the tuberculosis curve, it is evident that they are diverging persistently. The rate curve of cancer is observed to be rising but not so rapidly as the curve of heart disease.

In the United States Registration Area in 1925 the heart disease mortality rate per 100,000 was only 186, but this curve, too, was above all others, though not so much above as was the curve in New York State. The death rate for tuberculosis is fifth in importance in the United States Registration Area, but is seventh in the State, including accidents. Heart disease accounts in New York State for 21 per cent of all deaths, but in the United States Registration Area for only 15 per cent of deaths.

TABLE I

DEATH RATES PER 100,000 FROM SEVEN PRINCIPAL CAUSES OF DEATH

New York State Exclusive of New York City
1917-1926

CAUSE OF DEATH	1926	1925	1924	1923	1922	1921	1920	1919	1918	1917
Diseases of the Heart	303	273	261	270	260	234	243	221	247	251
Cerebral Hemorrhage	126	120	131	128	132	128	127	123	126	127
Cancer	121	121	120	117	115	114	109	106	104	103
Nephritis	121	118	112	111	111	110	117	116	128	136
Pneumonia	117	98	92	115	109	85	138	129	293	161
Accidents	86	89	88	90	82	76	78	76	88	97
Tuberculosis	85	89	91	95	95	99	112	126	145	138

*Read at the Fifth Annual Scientific Session of the American Heart Association, in Minneapolis, June, 1928.

†The detailed report of this study has been published in pamphlet form by the Medical Society of the State of New York.

If now the deaths for six leading causes of death are plotted (Tables II-A and B, and Fig. 2) by small age groups, the order of importance appears to be heart disease, cancer, cerebral hemorrhage, nephritis, pneumonia, and tuberculosis. Another interesting fact is that the number of deaths (Table II) from heart disease (14,480) is greater than the total number of deaths from both cancer (6,417) and tuber-

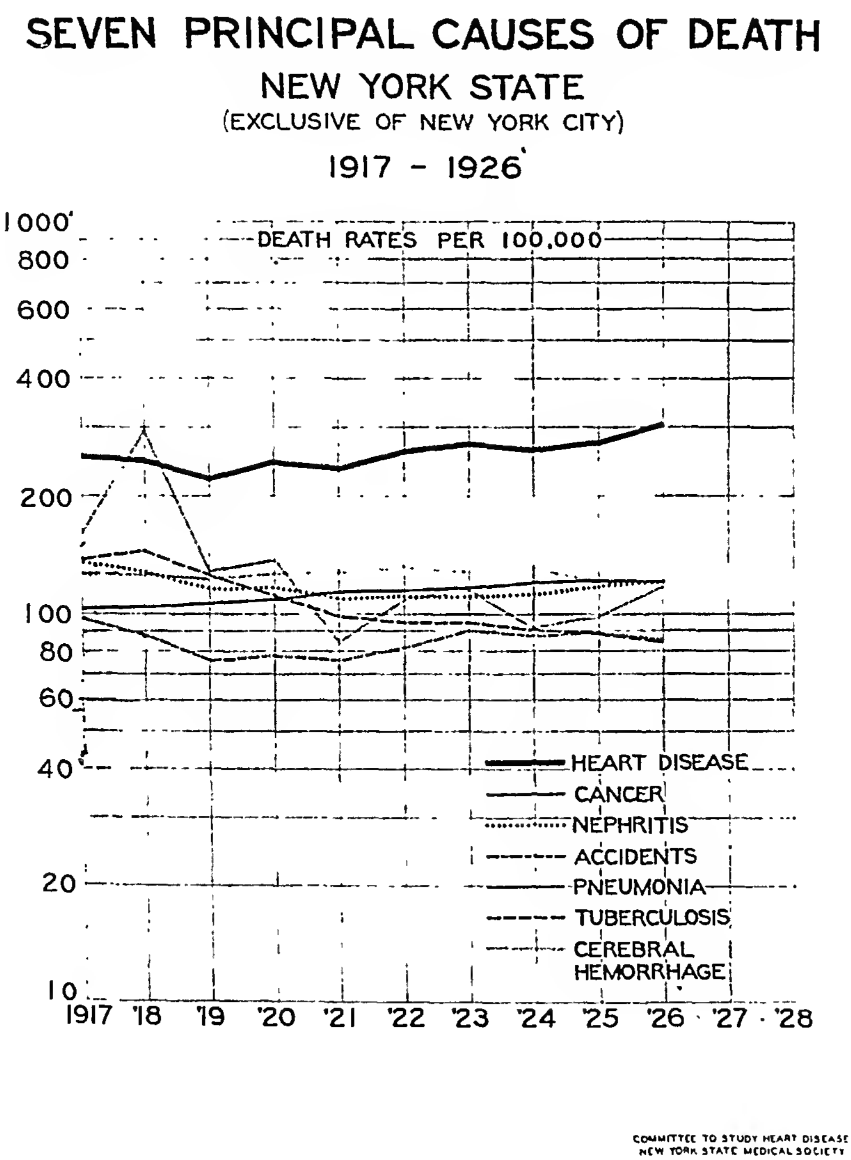

Fig. 1

culosis (4,698). In the United States Registration Area deaths from heart disease do not equal the sum of the deaths from cancer and tuberculosis.

The greatest number of deaths from heart disease, cerebral hemorrhage, and pneumonia occurs in the age group seventy to seventy-four years, while the greatest number of deaths from cancer and nephritis

TABLE II-A

DEATHS FROM SIX LEADING CAUSES BY AGE GROUPS

New York State Exclusive of New York City
1915

AGE GROUPS	DISEASES OF THE HEART	CANCER	CEREBRAL HEMORRHAGE	NEPHRITIS	PNEUMONIA	TUBERCULOSIS
All Ages	14,480	6,417	6,332	6,259	5,174	4,698
Under 5	116	14	25	37	1,298	215
5-9	89	7	4	19	87	63
10-14	126	8	7	19	66	62
15-19	121	8	5	40	81	345
20-24	114	24	10	43	102	559
25-29	135	43	13	46	116	621
30-34	163	80	24	105	149	596
35-39	269	157	46	159	200	464
40-44	422	296	105	230	258	373
45-49	583	439	184	322	257	326
50-54	826	613	346	414	275	277
55-59	1,059	804	469	549	261	203
60-64	1,481	873	721	676	343	213
65-69	1,904	948	940	886	403	170
70-74	2,103	875	1,134	865	411	112
75-79	2,078	663	1,029	821	338	60
80-84	1,624	376	758	617	295	29
85-89	888	139	358	282	153	5
90 and Over	371	47	152	123	78	1
Unknown	8	3	2	6	3	4

TABLE II-B

DEATHS FROM SIX LEADING CAUSES BY AGE GROUPS

New York State Exclusive of New York City
1915

AGE GROUPS	DISEASES OF THE HEART	CANCER	CEREBRAL HEMORRHAGE	NEPHRITIS	PNEUMONIA	TUBERCULOSIS
All Ages	10,820	4,649	5,440	6,068	6,288	6,195
Under 5	130	9	28	115	1,928	398
5- 9	72	11	4	26	90	99
10-14	90	7	1	20	49	116
15-19	87	9	4	41	70	422
20-24	98	19	9	87	118	748
25-29	147	36	17	111	126	758
30-34	177	83	29	135	134	690
35-39	234	145	62	203	179	644
40-44	313	253	106	250	239	552
45-49	437	381	190	366	255	456
50-54	614	517	306	467	278	395
55-59	826	584	503	544	317	292
60-64	1,085	601	609	680	407	235
65-69	1,382	668	733	794	432	157
70-74	1,697	541	908	783	513	117
75-79	1,529	428	905	699	479	68
80-84	1.120	239	608	484	376	37
85-89	572	81	309	200	194	10
90 and Over	210	36	109	60	104	1
Unknown	--	1	---	3	---	--

occurs in the age group sixty-five to sixty-nine years. The number of deaths from tuberculosis has diminished and the highest point of the curve is in the age group twenty-five to twenty-nine years, after which the curve falls persistently. The deaths from tuberculosis considerably exceed those from heart disease until the age of forty, after which time the deaths from heart disease far exceed those from tuberculosis.

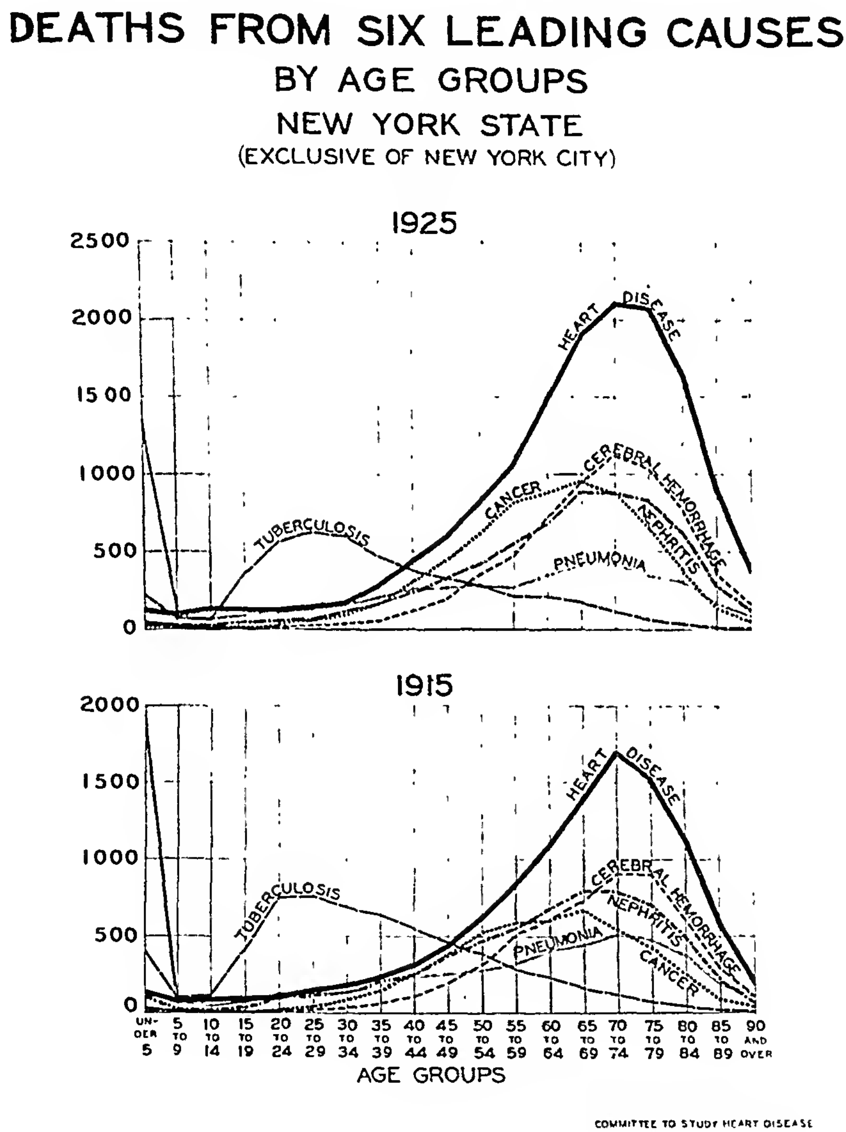

Fig. 2.

If now the comparison is made by cumulative percentage (Table III and Fig. 3) of the population, all deaths, and deaths from heart disease, by small age groups, certain interesting facts become apparent.

First, 50 per cent of the population is under the age of thirty years, while 50 per cent of the deaths from all causes occur under the age of sixty. The curve of heart disease deaths for 1925 has moved toward

TABLE III

CUMULATIVE DISTRIBUTION BY AGE GROUPS OF HEART DISEASE DEATHS FOR 1915 AND 1925

With All Deaths and Population for 1925

New York State Exclusive of New York City

AGE	HEART DISEASE DEATHS 1925 NUMBER	HEART DISEASE DEATHS 1925 PER CENT	HEART DISEASE DEATHS 1915 NUMBER	HEART DISEASE DEATHS 1915 PER CENT	ALL DEATHS NUMBER	ALL DEATHS PER CENT	POPULATION NUMBER	POPULATION PER CENT
Under 5	116	0.8	130	1.2	9,361	13.3	510,312	9.6
" 10	205	1.4	202	1.9	10,410	14.7	1,013,528	19.2
" 15	331	2.3	292	2.7	11,217	15.9	1,471,466	27.8
" 20	452	3.1	379	3.5	12,439	17.6	1,844,226	34.9
" 25	566	3.9	477	4.4	14,077	19.9	2,229,356	42.1
" 30	701	4.8	624	5.8	15,871	22.5	2,656,823	50.2
" 35	864	6.0	801	7.4	17,951	25.4	3,077,047	58.2
" 40	1,133	7.8	1,035	9.6	20,398	28.9	3,485,300	65.9
" 45	1,555	10.7	1,348	12.5	23,279	33.0	3,842,077	72.6
" 50	2,138	14.8	1,785	16.5	26,680	37.8	4,182,673	79.1
" 55	2,964	20.5	2,399	22.2	30,722	43.5	4,484,165	84.7
" 60	4,023	27.8	3,225	29.8	35,486	50.2	4,727,678	89.3
" 65	5,504	38.0	4,310	39.8	41,326	58.5	4,935,467	93.3
" 70	7,408	51.2	5,692	52.6	48,132	68.1	5,080,693	96.0
" 75	9,511	65.7	7,389	68.3	55,188	78.1	5,179,213	97.9
" 80	11,589	80.1	8,918	82.4	61,623	87.2		
" 85	13,213	91.3	10,038	92.8	66,688	94.4		
" 90	14,101	97.4	10,610	98.1	69,407	98.3		
All Ages	14,472	100.0	10,820	100.0	70,642	100.0	5,291,323	100.0
Unknown	8						4,337	

TABLE IV

PERCENTAGE DISTRIBUTION OF TYPES OF HEART DISEASE BY AGE GROUPS

For New York State Exclusive of New York City

1925

AGE GROUP	ALL FORMS	FORMS OF HEART DISEASE: PERICARDITIS	ENDOCARDITIS AND MYOCARDITIS	ANGINA PECTORIS	OTHER FORMS
All Ages	14,480	0.3	3.8	7.4	88.5
Under 5	116	1.7	35.4	0.0	62.9
5-14	215	1.4	31.6	0.0	67.0
15-24	235	0.4	31.1	0.4	68.1
25-44	989	0.5	17.5	5.9	76.1
45-64	3,949	0.2	2.6	11.0	86.2
65 and Over	8,968	0.3	1.1	6.4	92.2
Unknown	8				

the right, or older age side of the chart. Fifty per cent of the deaths from heart disease have not occurred until the age of seventy—ten years later than half the deaths from all causes. It is noteworthy that only 10 per cent of the deaths from heart disease have occurred at the age of forty-five years.

Ninety per cent of the deaths from heart disease occur after the age of forty-five. Heart disease then appears to be a disease of advanced

and old age, and it suggests that the prolongation of life may be a factor in the inereasing number of deaths aseribed to eardiae disease.

The grouping of the types of heart disease by pereentage distribution (Table IV and Fig. 4) shows 88.5 per cent of all the deaths to fall in "Other Forms" (No. 90) of the International List. Only 3.8 per cent of deaths fall in the group endocarditis and myoearditis (acute); with 35.4 per eent occurring under five years and 31 per eent

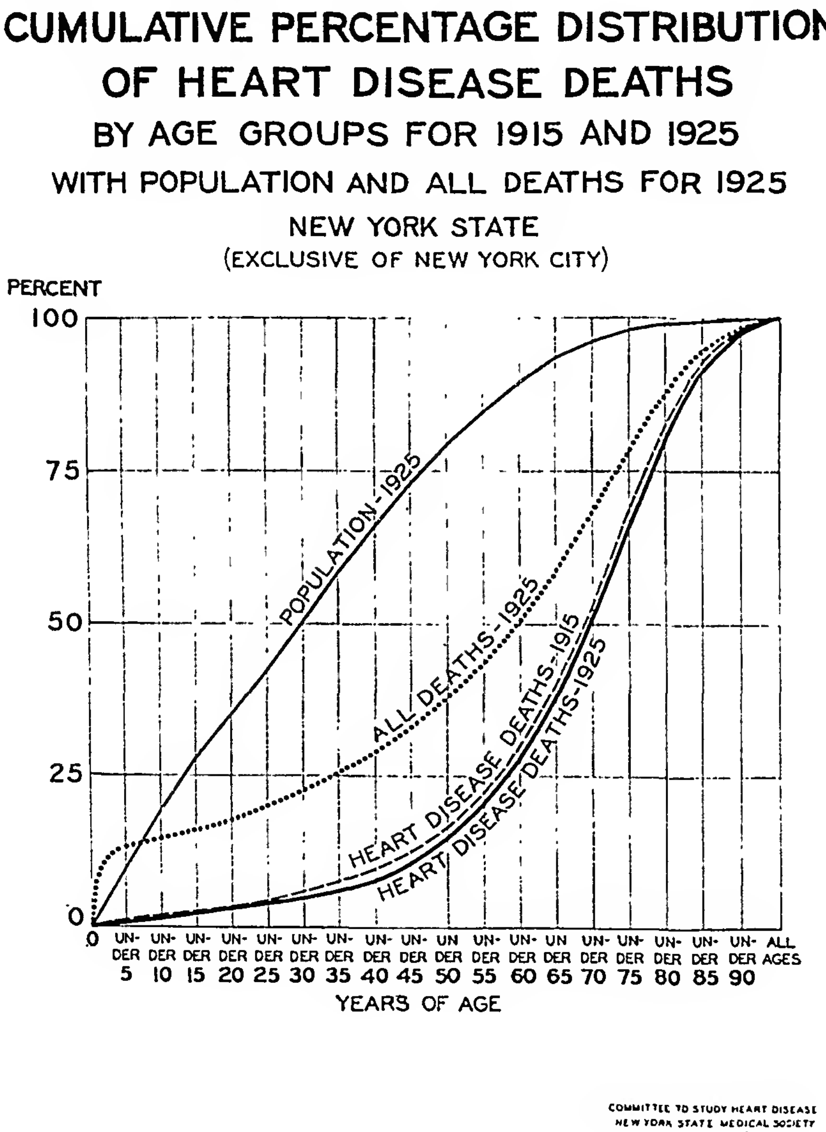

Fig. 3.

each in the age groups of five to fourteen and fifteen to twenty-four. These pereentage distributions are what one meets in praetiee but the numerical insignificanee of the whole group is astonishing, partieularly in view of the very scanty analysis of the group "Other Forms" which comprises over 88 per cent of all the deaths from heart disease.

"Other Forms" is officially divided into five headings: ehronie

valvular disease, aortic insufficiency, chronic endocarditis, chronic myocarditis, and fatty degeneration; but selecting the diagnoses under which most of the certificates group themselves, it appears that there are really ten headings (Table V), which differ, however, from those of the official list. These ten were studied.

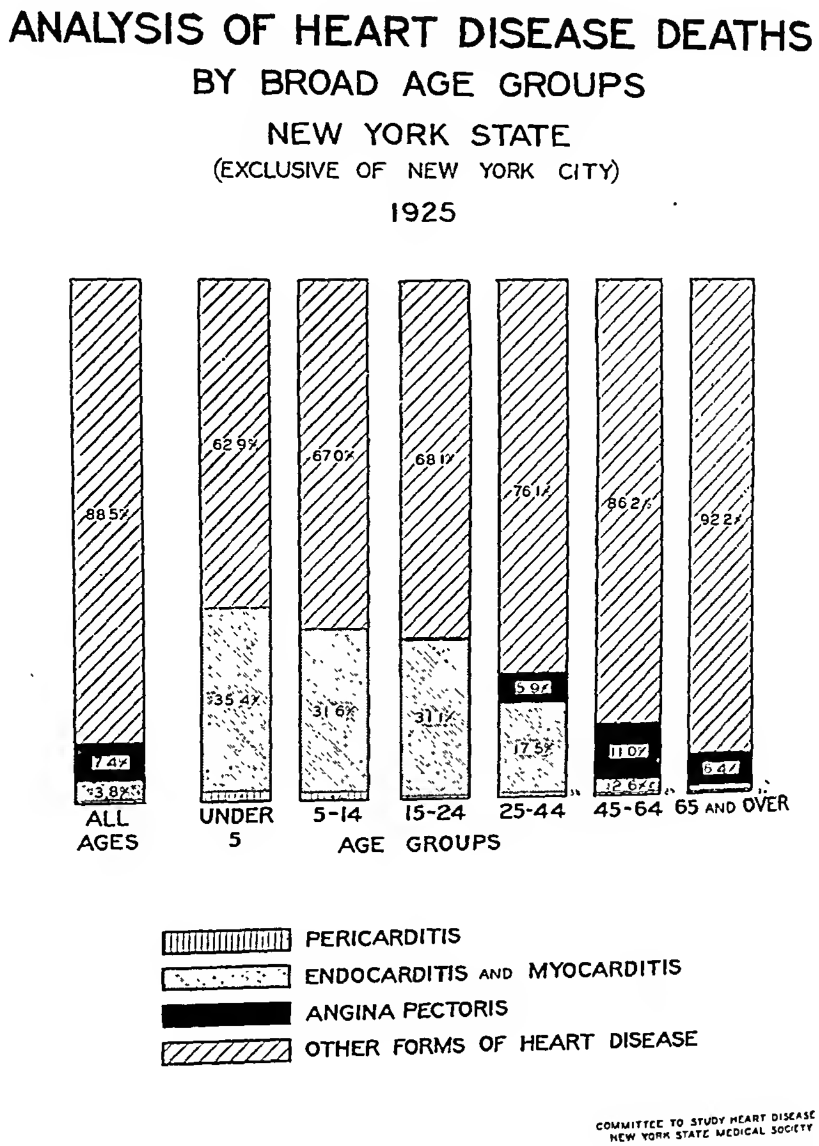

Fig. 4.

The striking fact is evident at once that the column "Chronic My carditis" includes nearly half of all the diagnoses in 1926, while 1922 it accounted for only slightly over one-third (34.1 per cent The column "Valvular Disease," which in 1922 contained nearly o quarter (23 per cent), now has only slightly over 15 per cent (15.7 The other subgroups show in 1926 only a slight decrease from t figures of 1922. It seems justifiable, therefore, to infer that the has been a trend in the fashion of diagnosis from the valvular lesio

TABLE V

OTHER DISEASES OF THE HEART. NUMBER OF DEATHS BY BROAD AGE GROUPS AND PERCENTAGE OF DEATHS FROM EACH TYPE

New York State Exclusive of New York City
1926

AGE GROUPS	TOTAL DEATHS	PERCENTAGE									
		CHRONIC MYOCARDITIS	CHRONIC ENDOCARDITIS	VALVULAR DISEASE OF THE HEART	MITRAL REGURGITATION	MITRAL STENOSIS	CARDIAC INSUFFICIENCY	DISEASES OF THE AORTA	CARDIAC HYPERTROPHY AND DILATION	CARDIORENAL DISEASES	OTHER DISEASES OF THE HEART
All Ages	14,862	48.6	12.4	15.7	3.6	1.4	4.8	2.1	3.4	0.7	7.8
Under 5	75	4.0	6.7	32.0	5.3	4.0	18.7	4.0	13.3	–	12.0
5 to 14	117	7.7	33.3	32.5	9.4	5.1	5.1	0.9	3.4	–	2.6
15 to 24	183	12.0	27.3	28.4	2.7	4.4	8.2	2.2	4.9	–	9.9
25 to 44	717	28.7	19.5	19.0	4.5	4.9	6.6	3.3	5.6	0.8	7.1
45 to 64	3,717	46.2	13.9	15.4	3.0	1.6	4.4	2.4	5.0	0.7	7.4
65 and Over	10,049	52.4	10.9	15.0	2.9	0.9	4.6	1.9	2.6	0.7	8.1
1922											
All Ages	11,509	34.1	13.0	23.0	4.4	1.3	5.1	2.5	4.8	1.3	10.5
Under 5	109	2.7	5.5	40.4	3.7	0.9	16.5	1.8	12.8	–	15.6
5 to 14	125	3.2	27.2	33.6	10.4	4.8	12.8	1.6	3.2	–	3.2
15 to 24	157	9.6	28.0	18.5	9.5	5.1	8.3	4.5	8.9	0.6	7.0
25 to 44	651	14.7	17.1	29.0	5.1	4.8	6.6	3.2	9.8	0.6	9.1
45 to 64	2,777	29.9	12.9	24.3	4.5	1.3	4.5	3.2	6.4	1.5	11.5
65 and Over	7,686	38.8	12.2	21.8	4.1	0.8	4.8	2.2	3.7	1.3	10.3

to the lesions of the heart muscle. There has been dissatisfaction with the consideration of valvular lesions as a cause of death and chronic inflammation of the heart muscle has been preferred as an explanation. This preference accounts for the fact that a very large percentage of the deaths in the age groups after twenty-five fall within the column "Chronic Myocarditis." Pathologists tell us that chronic myocarditis is one of the relatively rare conditions to be found in the heart, fibrosis of the myocardium being much the more common finding; yet this latter diagnosis has not been used in death certificates frequently enough to form a group for consideration.

The review of the death certificates gathered from the four numbers of the International List reveals the fact that there is no statement whatever concerning the etiological factor of the diseased heart. Only the most common anatomical deformities, which may well be due to several causative agents, are named. It would seem, therefore, that before a logical statement as to the accurate number of deaths due to heart disease can be made, some way must be devised to tabulate the damage under etiological headings, such as those of rheumatic fever, syphilis, other bacterial infections, and senescence or arteriosclerosis. To accomplish this physicians must accept and use recognized crite-

ria for diagnosis which include three factors—those of etiology (active or inactive), of anatomical or structural defect, and of pathological physiology.

The statistician must then tabulate the various anatomical defects according to etiology, instead of, as at present, listing such anatomical defects as causative conditions.

In other words, if we are to learn anything about the causes of death from heart disease, we, as physicians, must make diagnoses which give the etiology of the heart damage; the statistician, responsible for the records of Boards of Health Bureaus of Statistics, must arrange his machinery to tabulate the facts.

(*For discussion, see page* 116.)

HEART FAILURE AND HYPERTHYROIDISM*

With Special Reference to Etiology

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FIVE hundred cases of hyperthyroidism personally examined during the past fifteen months at the Lahey Clinic have been reviewed for the purpose of answering the following questions which pertain to the etiology of heart failure in thyrotoxicosis.

First—Does thyrotoxicosis injure the healthy normal heart muscle or is a previously damaged heart necessary for the production of congestive heart failure in hyperthyroidism?

Second—Does thyrotoxicosis have a specific stimulating effect on the heart aside from the over-activity of increased work?

Third—Does hyperthyroidism cause hypertrophy and dilatation of the normal heart from increased work, or from a specific stimulating effect, or both?

In consideration of the first question, if it can be demonstrated that myocardial injury results from thyrotoxicosis, it can be safely assumed that congestive heart failure will eventually result from prolonged intoxication. Wilson[1] has examined the hearts of 21 patients with hyperthyroidism, 18 of which showed marked lipoid changes. These patients fall in the age group where degenerative changes are frequently seen, so that, unless some specific pathological change due to thyroid toxicity is demonstrated, we must rely more on clinical observation to arrive at the probable answer to this question. Hamilton[2] has stated that, in his opinion, thyroid toxicity has a selective action on certain individual hearts. Since he does not specify what is characteristic of these individual hearts, this conclusion cannot be accepted until more definite clinical data have been presented. As to previous cardiac injury precipitating heart failure, we would expect in a community where rheumatic heart disease is prevalent many cases of failure in hyperthyroidism associated with mitral stenosis. Furthermore, as the age advances in which we find congestive heart failure, we should expect to find a considerable number with associated arteriosclerotic and hypertensive changes.

Concerning the second question, that of a specific stimulating effect of thyrotoxicosis on the heart aside from the increased work present, clinical observation supports this supposition. In many patients who have lost most signs of toxicity, and whose pulse and basal metabolic rates have returned to normal as the result of iodine administration

*From the Lahey Clinic, Boston, Mass.
Read before the American Heart Association at Minneapolis, June 12, 1928.

and rest, the characteristic thyroid thrust of the heart is often present far out of proportion to the then present demands of the circulation. The thyroid gland has undergone involution, the bruit disappears, the low diastolic pressure returns to normal limits, and still the thrust remains. As Willius and Boothby have pointed out[1] in other conditions where the basal metabolic rate is increased as in leucemia, or in moderate exercise, such as walking, the heart impulse is barely if at all palpable. This specific stimulation of the heart is, we believe, an important secondary factor in the production of cardiac failure.

In regard to the third question, Boas[3] believes that cardiac hypertrophy in hyperthyroidism is the result of increased oxygen demands and the increased flow through the thyroid gland. The latter he compares to an arterio-venous aneurysm or shunt. Read[4] believes that increased metabolic rate adds to the work of the heart and, if long continued, will result in myocardial failure. It is our impression, based on repeated teleroentgenograms—and others, I believe, are of the same opinion[1, 5]—that cardiac hypertrophy is rare in hyperthyroidism, except in a certain group of cases and in these it can usually be explained by coexistent cardiovascular disease. Our experience has been that the heart is too often considered enlarged because of the characteristic thrust and the movement of the thoracic cage. As a rule, the thyroid heart found in the patient dying of hyperthyroidism is flabby,[1, 6] and this impression is also gained by fluoroscopy. Such a condition would be consistent with some dilatation and we feel that the functional systolic murmurs so frequent in hyperthyroid hearts cannot adequately be explained on any other basis. Such dilatation and flabbiness are not characteristic of work hypertrophy, but is more consistent with the general muscular weakness which is so characteristic of thyroid over-activity.

CLINICAL DATA

Of the 500 cases of hyperthyroidism, 479 were of the exophthalmic type and 21 were of the toxic adenomatous type. The usual criteria were used in establishing the clinical diagnosis of hyperthyroidism and all cases studied showed confirmatory pathological changes in the gland removed at operation.

The criteria for diagnosis of cardiac changes were as follows:

1. Rheumatic heart disease with mitral stenosis was diagnosed only when a well-defined mitral diastolic murmur was evident.

2. Questionable rheumatic heart disease was diagnosed when there was a harsh apical systolic murmur, often a rheumatic history and usually some degree of enlargement.

3. Hypertension was diagnosed in the presence of a blood pressure of 190/90 mm. or more, or with a diastolic pressure of 100 mm. or more, regardless of the systolic pressure.

4. Arteriosclerosis was considered present when there was well-marked hypertrophy, tortuosity, and hardening of the peripheral vessels.

5. Luetic aortitis was diagnosed when an aortic regurgitant murmur was present along with a positive Wassermann. (The two cases included both had dilated aortic arches.)

6. Established auricular fibrillation was diagnosed when this irregularity remained present from the time of admission to the hospital until operation.

7. Paroxysmal auricular fibrillation occurred in most cases postoperatively, and was diagnosed only when personally observed.

8. Transient congestive heart failure. All patients having a clear-cut history of past failure relieved by rest and iodine before coming under our observation were placed in this group.

9. Paroxysmal tachycardia and auricular flutter were identified by the electrocardiogram.

10. True congestive heart failure. All of these patients had pitting edema of the legs, the neck veins were always distended in the upright position and the liver edge was down. Orthopnea of varying degrees was present. The degree of failure varied, of course, some clearing with rest and iodine, while others required the use of digitalis and diuretics.

TABLE I

CLASSIFICATION OF HEARTS IN 500 CASES OF HYPERTHYROIDISM

TYPE	NUMBER OF CASES	AVERAGE AGE IN YEARS	DURATION OF HYPERTHYROIDISM IN MONTHS
I. No change	339	35	17 mo.
II. Paroxysmal auric. fibrillation	20	49	12 mo.
With heart changes	20		
III. Probable rheumatic heart	14	27	13 mo.
With failure and auric. fibrillation	2	42	(7 mo.-8 yr.)
IV. Rheumatic heart	21	35	11 mo.
With failure and auric. fibrillation	2	50	11 mo.
V. Established auricular fibrillation	36	49	14 mo.
(3 hypertensive) (all types)	56	53	16 mo.
VI. Transient congestive failure			
Normal rhythm (4 hypert.)	13	42	7 mo.
With est. aur. fib. (1 hypert.)	3	57	8 mo.
VII. Hypertensive heart	24	54	18 mo.
With luetic aortitis	1		
VIII. Cardiac hypertrophy ? of cause—no failure	4	60	10 mo.
IX. Angina pectoris (1 hypert.)	2		
X. Paroxysmal tachycardia	2		
XI. Auricular flutter	2		
XII. Congestive heart failure	26		
(a) Rheumatic	2	50	11 mo.
(b) ? Rheumatic	2	42	(7 mo.-8 yr.)
(c) Arteriosclerotic and hypertensive	13	54	28 mo.
(d) Luetic (included in above)	1		
(e) ? Cause	9	51	38 mo.*
Total C. H. F.	26	49	

*The duration in this group showed a mean of about 18 months; two patients dated their onset 8 and 12 years but in each case it was questionable.

DISCUSSION

There are certain very obvious facts to be noted from this tabulation. In the first place, the duration of the hyperthyroidism does not seem to play a consistent part in the production of auricular fibrillation, or of congestive heart failure. The basal metabolic rate varied considerably and showed no relation to the degree of congestive heart failure. No attempt was made to correlate the basal metabolic rates because of the frequent iodinization before coming under our observation.

Of importance we feel is the freedom from congestive heart failure in the group with mitral stenosis. On the assumption that previous myocardial damage is necessary to precipitate failure in hyperthyroidism, this finding is rather surprising. On the other hand, the average age of this group is the same as those cases which we considered as having no heart changes. This brings up the important point of age, which we will again emphasize as being a paramount factor in the production of congestive failure in hyperthyroidism.

The low average age of the questionable rheumatic heart group serves to confirm the clinical diagnosis which was made in these cases. Here again those showing failure were far above the average age of all the rheumatic cases.

It is interesting to note in regard to age that we find more heart disturbances (particularly established or paroxysmal fibrillation) as we approach fifty years. The average age of the established auricular fibrillation group was forty-nine, while in those showing congestive heart failure with this irregularity it was above fifty years. One-third of the total of 36 cases with hypertension showed frank congestive heart failure. Here again we note the factor of age, for the average of this group is fifty-four years. Those patients showing well-marked arteriosclerosis had an average age of fifty-six years; of these patients four were males. If arteriosclerosis were more common in females, we feel that we would see a greater number of cases showing congestive heart failure. In the 26 cases of congestive heart failure 17 showed definite hypertensive or arteriosclerotic changes.

The remaining 9 cases in the congestive failure group, in so far as could be determined, showed no evidence or gave no history of coincident cardiovascular disease. These patients showed many features in common. Cardiac enlargement was present in most instances and by x-ray the enlargement was often shown to be both to left and right. Electrocardiograms showed no preponderance of either ventricle; low voltage was seen in half the cases and auricular fibrillation was present in the majority. Congestive failure was not of the extreme type, having been improved in all cases by rest, iodine, and (occasionally) digitalis.

Sufficient time to form a final opinion as to the end-results in all the congestive failure cases in this group has not elapsed, but previ-

ous experience gives us the impression that the prognosis in each case depends on the amount of coexisting cardiovascular disease present. Three of the failure group herein reported are dead. One died of pneumonia before operation, another died of congestive heart failure five months after operation, having had hypertensive and rheumatic heart disease, and a third died suddenly after four months of comparative freedom from cardiac disability.

CONCLUSIONS

From the data presented what conclusions can we draw in regard to the etiology of congestive heart failure in hyperthyroidism?

First, if thyrotoxicosis injures the normal healthy heart we believe there should be more evidence of injury below the age of forty. The average age of the congestive heart failure group being above fifty years, with a large percentage showing coexisting cardiovascular disease, leads us to conclude, on a clinical basis at least, that if there is a selective action of hyperthyroidism it chooses the heart in patients who are over forty years old. If auricular fibrillation is to be considered evidence of myocardial damage from thyrotoxicosis, it certainly should be present more often in the younger patient and particularly should it have a more definite relationship to duration and degree of toxicity.

The nine cases showing no clinical evidence of coexisting cardiovascular disease, present an important group in regard to the question of myocardial injury as the result of thyrotoxicosis. Because of the small number of patients and their advanced age we feel we cannot attribute their heart failure to thyrotoxicosis directly, but believe that these patients have some unrecognized myocardial weakness either from previous unknown injury or because they belong to that group of individuals who inherit a predisposition to cardiovascular degeneration. The drive of hyperthyroidism serves to bring out this inherited weakness, and although the average duration of the disease is somewhat longer in this group, this seems a natural explanation in view of the lack of gross clinical evidence of more advanced cardiovascular disease.

Second, we believe that thyrotoxicosis has a specific excitatory effect on the heart and that this, more than the increased work from circulatory demands, produces failure in a heart weakened by the degenerative processes of age.

Third, our clinical observation leads us to believe that hypertrophy of the heart does not take place in a normal healthy heart as the result of hyperthyroidism, but that dilatation is probably frequent. Duration, we feel, plays a very little part in a general way. It is obvious, however, from frequent examinations of thyroid patients that duration as well as degree of toxicity plays an important rôle in individual

cases. Immediate removal of thyroid toxicity by surgical procedure is undoubtedly the quickest and surest method of averting the onset of congestive heart failure.

Therefore, in conclusion, we consider the most significant causes of congestive heart failure in hyperthyroidism: (1) age and the coexisting cardiovascular changes associated with it; (2) the specific heart drive incited by thyrotoxicosis; (3) auricular fibrillation; (4) duration and intensity of thyroid overactivity.

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[6]Smith, L. W.: Personal communication.

(For discussion, see page 116.)

THE DISTORTION OF THE ELECTROCARDIOGRAM BY CAPACITANCE*

A Critical Analysis of the Electrical Amplification of Heart Currents

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THE introduction of a condenser (electrical capacity or capacitance) in series with the leads from the patient to the string galvanometer has a well-known effect in distorting the electrocardiogram. The relations of this effect to polarization of electrodes, to skin changes in myxedema, and its use in obviating the need for a variable current to

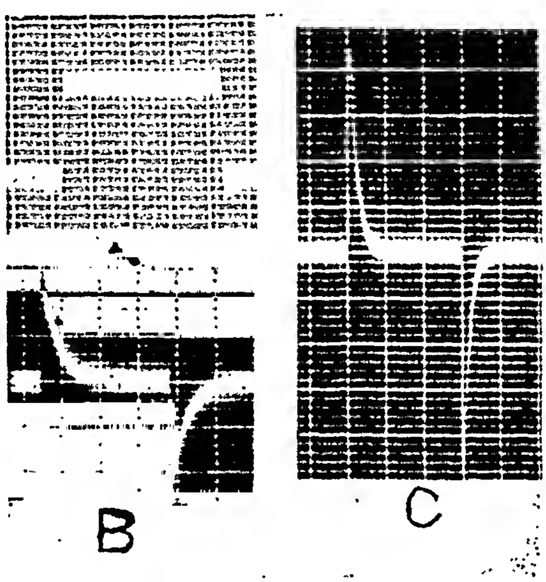
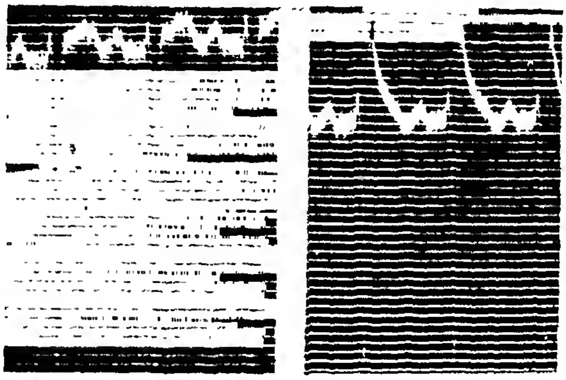


Fig. 1.—*A*. The normal make and break curve of the string galvanometer. External resistance 3200 ohms.
B. The same, with 20 microfarad capacity in the circuit, string returns one-half distance to zero in 0.07 seconds.
C. The same, external resistance reduced to 500 ohms, one-half decrement period reduced to 0.04 seconds. On the break, in *B* and *C*, the string moves in the opposite direction to the make.

neutralize skin currents are known to all who are familiar with electrocardiography. The recent introduction of resistance-and-capacitance-coupled amplifiers into electrocardiographic technic calls for a reconsideration of this distortion, as the only descriptions of these instruments[1, 2] give no critical data bearing on this point. Many of the users of these new instruments are more or less unfamiliar with this distortion and have made no extensive comparison of their instruments with the string galvanometer.

*From the Medical Clinic of the Stanford University Medical School, San Francisco.

A capacitance, introduced into an electrical circuit, impedes direct flow of current, but permits surge in the line. Fig. 1 shows the effect of a capacity on the curve due to make-and-break of a constant current applied to a string galvanometer. At the make the normal deflection occurs, but is not sustained; the return to the zero line occurs at a rate inversely proportional to the circuit resistance and to the size of the capacity. On the break, the string moves in the opposite direction due to the surge in the line and again returns to the base line. In Fig. 2 the distortion of the electrocardiogram produced by a capacitance is clearly shown because the unusually large QRS deflection accentuates the effect. In Fig. 3 is shown the effect of make-and-break, and of a current of brief duration on the record made by a very good amplifier-type electrocardiograph. Control tests of make-and-



A. *B.*

Fig. 2.—*A.* Normal curve (Lead III) of a person with left axis deviation.
B. The same, after introducing 20 microfarad capacity into circuit. Note shortened S-wave and distortion of S-T due to capacitance.

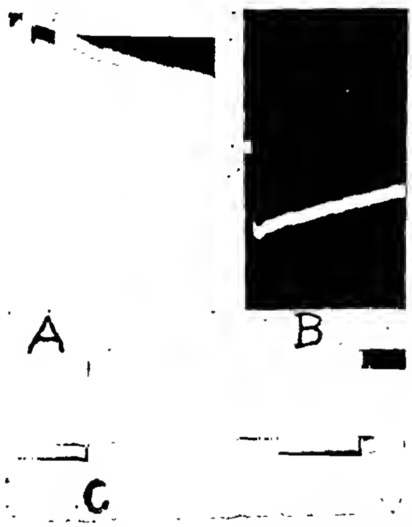


Fig. 3.—*A.* Make of 1 millivolt current (3200 ohms external resistance) as recorded by a three-tube amplifier electrocardiograph, period of one-half decrement is 1.35 sec.
B. Break of same current in same instrument.
C. Rapid make and break; *note overshooting* of base line even with current of short duration and one millivolt amplitude.

break with the galvanometer of this instrument showed curves similar to Fig. 1-A. It will be noted that the period needed for 50 per cent return to zero after make is twenty times as long as with the string galvanometer with a 20 microfarad capacitance. The latter shows but little distortion of normal tracings and is satisfactory and routinely used in this laboratory for experimental observations on small animals and birds. While the amplifier-type instrument is far more accurate than the combination just mentioned, it does distort an important part of the electrocardiogram, as shown by the overshooting past the zero line on "break" in Fig. 3, and by a comparison of the true (string galvanometer) curves with those recorded by this instrument on the same patient (Fig. 4). The terminal part of

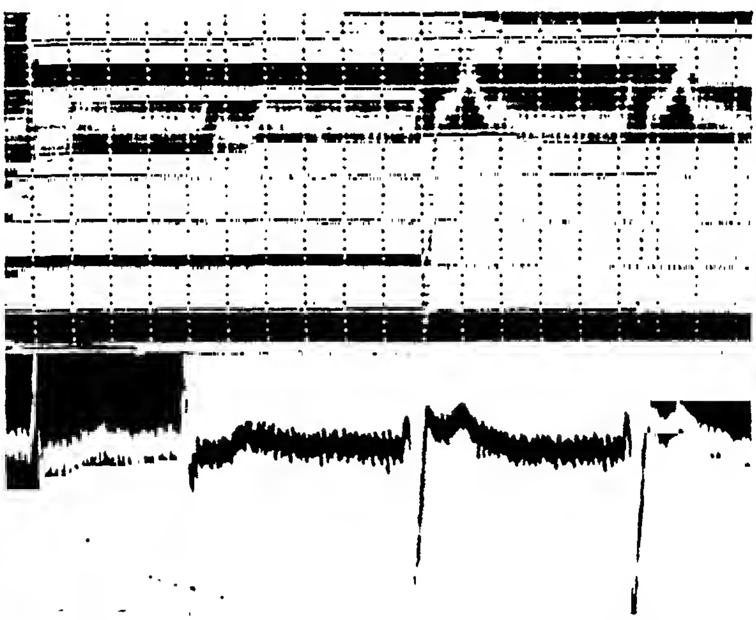


Fig. 4.—Upper curve, string galvanometer record. Lower, three-tube amplifier electrocardiograph record. Note the exaggerated S and flattened T of the first two beats, the marked S-T distortion of the last two beats.

the QRS and onset of T are distorted in the same way although to a less degree than in Fig. 2. To those who are interested, not merely in relation of events in the cardiac cycle, electrical axis deviation, and the like, but also in the details of the ventricular complex, the present amplifier-type electrocardiographs are therefore unsatisfactory. The ventricular complex distortion increases in proportion to the duration and voltage of the QRS deflection. It may conceal changes due to coronary disease, or produce distortion suggestive of such changes in patients whose QRS is of high voltage.

SUMMARY

Capacitance, introduced into the circuit with a string galvanometer or incorporated into an amplifier for heart currents, distorts the ven-

tricular complex. This distortion increases with decrease in resistance and capacitance in the circuit, and with increase in the voltage of the QRS deflection. Electrocardiographic tracings made with amplifier-type instruments can only duplicate accurate string galvanometer tracings when make-and-break test currents give records similar to those of the Einthoven electrocardiograph. The usual distortion of the QRS complex, due to capacitance in the amplifier, is slight but must be considered in reading the tracings produced by the instruments now available.

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THE USE OF FAHNESTOCK CLIPS IN THE TECHNIC OF TAKING ELECTROCARDIOGRAMS*

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A YEAR ago, acting on the suggestion of Herrmann and Wilson[1] we began to use flexible copper wire as electrodes in taking electrocardiograms on patients in the clinic and on animals in the laboratory. We have found this electrode satisfactory both from the point of view of consistently obtaining low skin resistances and also because of ease of application. Herrmann and Wilson used double connecting binding posts to connect the lead wires to the copper wires. In the routine use of double binding posts we frequently found that the screws of the binding posts were not adjusted tightly. This resulted in distortion of the electrocardiogram and waste of time in making readjustments. It occurred to us to substitute brass Fahnestock clips† (Fig. 1) for the double connecting binding posts. The spring clip automatically makes a tight connection. The adjustment is much quicker than the use of binding posts with screws. The clips can be left attached to the lead wires.

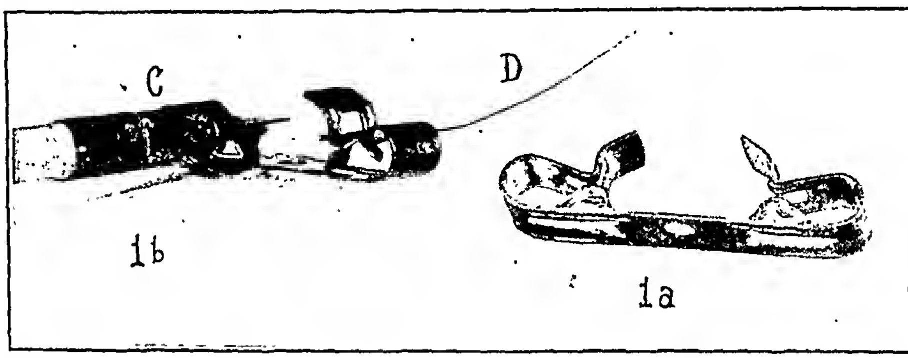

Fig. 1-a.—A photograph of a Fahnestock clip. 1-b, shows the lead wire (*C*) connected to one of the Fahnestock clips and copper wire (*D*) used as the electrode connected to the other end. One-half natural size.

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*From The Hospital of the Rockefeller Institute for Medical Research, New York.

†Fahnestock clips have come into extensive use in wiring radio apparatus. They can be obtained for 5 to 10 cents per clip. They last indefinitely. If, from repeated use, the spring becomes pushed down too far so that the small guage wire does not fit tightly under the clip, the spring can be spread.

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Official Organ of the American Heart Association

Coordination of Investigation

A COMMITTEE of the American Heart Association, known as the Committee for the Coordination of Investigation, was organized in October, 1927, for the purpose of fostering collective research in the more definitely medical and scientific aspects of heart disease, and has decided upon a definite program for research to occupy the coming year. The committee consists of seven members, Dr. Edward C. Carter of Baltimore, Dr. Cary Eggleston of New York, Dr. Edward B. Krumbhaar of Philadelphia, Dr. H. M. Marvin of New Haven, Dr. Paul D. White of Boston, Dr. Frank N. Wilson of Ann Arbor, and Dr. Harold E. B. Pardee of New York, who is the Chairman of the Committee.

A schema for the study of cardiovascular syphilis has been elaborated by this committee, and various interested workers throughout the country have been invited to take part in the study, thereby becoming contributing members of the committee. Up to the present time more than thirty men have signified their desire to take up one or more of the phases of this subject. With the cooperation of these numerous workers, it is confidently believed that this study should

result in a definite advance in our knowledge of the etiology, the pathology, the clinical diagnosis, and the treatment of syphilis of the heart and aorta.

The committee will be glad to increase the number of contributing members. Anyone wishing to take part in this investigation may make application to become a contributing member, and to do this should communicate with the chairman, outlining briefly the phase of the subject which he desires to cover. It is hardly possible to have too many investigators engaged in this work. No harm will be done, and probably much benefit will accrue, even if two or three men should be working on exactly the same problem. The agreement or the discrepancies in their findings might well be of much importance. The committee would be glad also to send to any one who is interested to receive it the schema which has been prepared, outlining the study of the subject as a whole. It is expected, not that any one person should investigate all the problems outlined in this schema, but that each man should select those which he is best fitted to attack, or those in which he has the greatest interest. The results of this investigation will be reported at the next annual meeting of the American Heart Association and will constitute the scientific session of this organization. It is hoped that the combined researches may be published in book form.

Society Transactions

AMERICAN HEART ASSOCIATION

FOURTH ANNUAL SCIENTIFIC SESSION

June 12, 1928

The fourth annual scientific session of the American Heart Association was called to order shortly after two o'clock on Tuesday, June 12, 1928, in the Ball Room of the Leamington Hotel in Minneapolis, Minnesota, as follows:

The Chairman, Dr. William H. Robey, Boston, Mass.—Ladies and gentlemen, we have waited, I think, as long as we can for our president, Dr. James B. Herrick of Chicago, who was to begin the meeting. I am sorry there is not a larger attendance. Some of the speakers would like to have a lantern, and I believe that one is being brought from somewhere—I think in this city—so that the first paper I will call for is by Dr. Hurxthal.

1. Dr. Lewis M. Hurxthal, Boston, Mass.—**Heart Failure and Hyperthyroidism.** (For original article see page 403.)

2. Dr. Robert H. Halsey, New York, N. Y.—**Observations on the Mortality of Heart Disease in New York State.** (For original article see page 94.)

3. Dr. Paul W. Emerson, and Dr. Hyman Green, Boston, Mass.—**Idiopathic Hypertrophy of the Heart in Infants.***

It would be better to designate the tremendous increase in the size of the heart described in the literature as ''idiopathic hypertrophy'' by the term, ''hypertrophy of unknown etiology,'' but so few cases have been reported that for the present, to keep the literature on the subject accessible, we have retained the old name. Such enlarged hearts described by Howland in his classical article showed hypertrophy and nothing else except in two instances a very small open foramen ovale. He was of the opinion that it was unjustifiable to discard a case as one of idiopathic hypertrophy merely because it showed likewise a simple defect. The two kinds of cases, hypertrophy with simple defect and hypertrophy without, are so similar clinically that one might, before post-mortem examination of the heart, swear as to the correctness of a diagnosis, only to find that without a murmur, a simple defect such as a foramen ovale, an open interventricular septum or a patent ductus arteriosus would be present, or that with a murmur nothing would be shown except a hypertrophy.

We believe that such cases of idiopathic hypertrophy which also have simple defects are worthy of reporting as a class and we have five such cases. With the purpose of emphasizing this class we are reporting six cases of idiopathic hypertrophy of the heart without other defect. In all of the cases the hearts were enlarged to from two and a half to four times the normal size, and in all of them

*Abstract of paper read at the Fifth Annual Scientific Session of the American Heart Association in Minneapolis.

dyspnea and cyanosis were the most common symptoms. The oldest patient was twenty-eight months of age. Seven died within one week after admission to the hospital. We could find no satisfactory etiology for this disease but we suspect that a possible and as yet uninvestigated cause may be a congenital narrowing of the capillary bed. There were eight autopsies.

4. Dr. B. J. Clawson, Minneapolis, Minn.—**Fibrosis of the Myocardium.** (See Myocarditis, page 1.)

5. Dr. Robert L. Benson, Portland, Ore.—**Rupture of the Heart.**

DISCUSSION

The Chairman.—This has been a most interesting group of speeches that has been presented this afternoon, and I will ask Dr. Albert to open the discussion.

Dr. Henry Albert, Des Moines, Iowa.—Mr. Chairman. From the public health point of view, which is the point of view in which I am interested, it is very encouraging to note the very great interest which is being manifested in the study of heart disease, not only by the public and the medical profession in general, but also by special groups, such as is, for instance represented by this association. The public has become interested the past few years, largely because heart disease is now the leading cause of death in this country, and mortality from heart disease also is, and for some years has been, on the increase.

On the other hand, the public health official meets with two great difficulties when it comes to heart disease. *First.*—Heart disease is not a definite thing like tuberculosis and typhoid fever. Heart disease varies so widely in its nature and is produced by such diverse causes, that the problem of evaluating the influence or effect of the several factors is a very complex and difficult one. *Second.*—Heart disease does not present the urgent call for immediate attention that we have in connection with diphtheria or scarlet fever or other readily communicable diseases. When you have to wait ten or fifteen years after the cause started to act before the disease forces itself on your attention, you can readily appreciate that the busy health officer is much more likely to look after quarantinable diseases and the paying public is much more interested in having the health department protect them from dangers immediately at hand.

I was much interested this afternoon, especially in the reference made by Dr. Halsey of the importance of securing certain statistical data. He suggested that the cause of heart disease be included on the death certificate. Now, I agree with him that it is very desirable to have more definite data than we now get. We who are gathering statistics in state public health departments are interested in having as definite data as possible with reference to the cause of disease, but as far as heart disease is concerned, the cause is not susceptible of being given in as definite a form as in connection with most other conditions, and certainly it is not as simple as would be implied by simply dividing it into rheumatic, syphilitic, and arteriosclerotic groups. We may speak rather definitely with reference to the rheumatic and syphilitic forms but when it comes to arteriosclerosis, we have here to deal with a pathological condition, or possibly as suggested by some, with a normal senescent process—rather than an etiological factor. When it comes to a case of arteriosclerosis we have to deal with many factors, some of which are as yet but poorly understood.

A year or so ago I delved into a certain speculative field. I got the notion that more cases of heart disease were caused by scarlet fever than it had been given credit for. Once having decided upon that notion I wanted to get the data to

substantiate the notion, and on the general supposition that most cases of scarlet fever probably cause a certain amount of injury—some causing a chronic nephritis; others chronic heart disease; and others, milder conditions. I desired to get this information in the form of statistics. At the present time there are many more people who have survived an attack of scarlet fever, and presumably been injured by the toxin liberated by the streptococcus which causes scarlet fever, than there were some years ago. Whereas in 1906 the scarlet fever morbidity rate was 112 per 100,000 population, in 1926 the rate was 268. On the other hand, in spite of this increase, or at least apparent increase, in the number of cases, the mortality rate has decreased from six per 100,000 population in 1906 to two in 1926. According to this, then, there were, in 1906 one hundred and six persons out of every 100,000 population who survived an attack of scarlet fever that particular year, whereas in 1926 there were 266 persons that thus survived—an increase of 150 per cent. When we consider that this increase has occurred in a rather progressive way almost every year since 1906, it means that the cumulative effect has been very great. I noticed in last week's *Journal of the American Association* a reference to a contribution on allergy made by Dr. Swift. I don't know just how that process works, but I hope that Dr. Swift is right, largely from the standpoint of substantiating my theory. I hope he finds that a considerable number of cases of heart disease are due to scarlet fever.

It is apparent that the solution of the heart disease problem requires not only careful research as to etiology, pathology, diagnosis and treatment, but that it also requires some long range public health statesmanship. I know of no problem in medicine that is in greater need of effective cooperative work between the pathologist, the clinician, and the public health official.

Dr. B. S. Oppenheimer, New York, N. Y.—Mr. Chairman, the paper of Dr. Emerson interested me because we have had a few such cases of hypertrophy of the heart in infants. We have no explanation to offer as to the cause. I recall one case. This was a boy born in 1920—certainly normal—and he died at the age of 19 months. About a week before he died he became very cyanotic. Attention was first attracted to the unusually large heart. Teleroentgenograms showed the huge heart he had. There were rapidly progressing symptoms of cardiac failure, from which he died. The autopsy revealed no pathological condition of the chest at all. The weight of the heart at 19 months was 125 grams. A normal heart for this age would be at most 50 grams. This weighed two and a half times as much as it should at that age. It was not a man's sized heart; it was the heart of a child of ten.

I should like to ask Dr. Emerson if there is any evidence that these cases live to adult life. As far as I know they have all been fatal. I should like to ask him, too, if it is possible that these cases may be due to the narrowing of the capillary bed, and whether that would explain the general hypertrophy of the heart.

I should like to speak for a moment also concerning Dr. Clawson's work. I think the difference between the statistics which Dr. Halsey presented and the figures from Dr. Clawson is accounted for by the fact that the doctors in the East call everything chronic myocarditis. Dr. Halsey's paper makes it clear that one should not apply the term myocarditis to myolysis. I think that distinction must be made in order to clear the question of diagnosis on death certificates.

Dr. Joseph Sailer, Philadelphia, Pa.—Myocarditis is an unsatisfactory diagnosis. Our medical students are taught to diagnose it too readily. Usually if the pulse and the heart sounds are weak and the patient is old, it is assumed. As a rule it is difficult to obtain confirmation from the pathological department.

I wish I could agree with Dr. Oppenheimer that myocardial changes can be recognized in the electrocardiogram. I have met only one case in which the tracing was of proved value. The patient was an old woman, and we diagnosed before her death that there was a thrombus in one of the branches of the coronary artery. This was subsequently demonstrated by filling the coronary circulation with metallic mercury and taking an x-ray.

Dr. Hyman Green, Boston, Mass.—Idiopathic hypertrophy of the heart has been confused with other chest conditions. It has been diagnosed tuberculous effusion and mediastinal newgrowth. In two cases to our knowledge a needle has been inserted into the chest, and in one case through the heart itself for what was thought to be a pericardial effusion. These cases have been known to us only a short time, but we feel that with the increased knowledge of blood pressure, the electrocardiogram, and x-rays we will better be able to diagnose this condition. The electrocardiogram is not as yet an absolute means of making the diagnosis, however, the curves are fairly characteristic. Our cases all died of heart failure. Digitalis was tried in a few but was absolutely of no avail.

The Chairman.—I have talked this matter over with Dr. Mallory, who assured me that acute inflammatory conditions of the heart muscle such as we get in rheumatism do the heart no material injury. It seems to me difficult to believe that you can have these minute scars in the heart without bringing on considerable trouble later in life, but I understood Dr. Clawson to say that it did not materially damage the heart, and other pathologists have insisted upon that also.

Is there any further discussion upon the papers we have listened to this afternoon? If there is none, I will entertain a motion to adjourn.

(Upon motion duly made and seconded the meeting adjourned.)

Department of Reviews and Abstracts

Selected Abstracts

Keefer, Chester S., and Resnik, William H.: Angina Pectoris. Arch. Int. Med., 1928, xli, 769.

In this paper the authors present a theory which explains the attacks of angina pectoris on a basis of localized anoxemia of the myocardium. They believe that the attack occurs when the oxygen supply to the heart is inadequate to meet the oxygen demands of the heart. In the usual case of angina, the anoxemia is relative, being sufficient for the needs of the heart at rest and insufficient when the work of the heart is increased. In acute coronary occlusion, however, the anoxemia is absolute, since the oxygen supply is inadequate, even when the heart is at rest.

Anoxemia of the myocardium may exist without causing angina. They point out that under these conditions when anoxemia affects all the tissues of the body as well as the heart, for example in pernicious anemia, or when the heart is uniformly affected so far as one may judge, angina is usually absent. When the heart is affected in such cases the symptoms are practically always those of so-called congestive heart failure.

On the other hand, angina tends to appear when in spite of anoxemia being present the contractural power of the heart remains good, evidenced by more or less complete freedom from dyspnea or other symptoms of a failing myocardium. These conditions occur most commonly when only a restricted part of the heart muscle suffers from lack of oxygen, as in coronary sclerosis. The remainder is relatively uninvolved and hence the contractural power of the heart remains good.

Parkinson, John, and Bedford, E. Evan.: Successive Changes in the Electrocardiogram After Cardiac Infarction (Coronary Thrombosis). Heart, xiv, 195.

Electrocardiograms are given from twenty-eight cases in which the diagnosis of cardiac infarction was made. Twenty-two patients are still alive and six have died; in four of the latter necropsies were obtained, each confirming the diagnosis.

The modifications of the ventricular complexes of the electrocardiogram following cardiac infarction are described in detail, and illustrated by serial records. Usually a definite sequence of changes in the R-T segment and in the T-waves is recorded. Shortly after the onset of symptoms a transient deviation of the R-T segment from the isoelectric plane occurs. This is followed by a deep inversion of the T-wave in either Lead I or Lead III, but not in both, and often by a lesser degree of T inversion in Lead II. Curves obtained after a few weeks conform to one of two main types according to the incidence of T inversion in Lead I or in Lead III. Subsequent T-wave changes in the direction of the normal are recorded, and even complete return to normal occurs. A negative T-wave in Lead III alone may be significant of past infarction.

T-wave changes seen in clinical curves are comparable with those observed

in experimental curves after coronary ligation, or after focal injury to the myocardium. The significance of modifications of the R-T segment and of the T-waves is discussed. The definite train of events seen in the electrocardiogram can be correlated with the pathological changes evoked in the myocardium by coronary occlusion. The R-T deviation indicates active spread of the area of necrosis. It is suggested that T-wave inversion indicates impairment of myocardial function in the area of distribution of the occluded artery, and that such impairment of function is not confined to the limits of the actual necrosis. The return of the T-waves toward normal corresponds to a progressive recovery of function of the myocardium in the territory of the occluded vessel. Such functional improvement can be explained by the development of a compensatory collateral circulation, by the increased circulatory efficiency and rise of blood pressure after recovery from shock and by the subsidence of edema and cellular exudation around the infarct.

Hume, W. E.: The Action of Adrenalin Chloride on the Human Heart. Quart. Jour. Med., 1928, xxi, 459.

The general effects of intravenous injections of small amounts of adrenalin chloride are considered. The electrocardiographic records are described from three individuals into whom a similar injection had been made and the effects of adrenalin chloride on the mechanism of the heart have been recorded. Two of the cases developed ectopic ventricular beats in regular repetition. One of the three cases showed transient auricular fibrillation.

Grant, R. T., and Jones, T. Duckett: A Case of Obstruction to the Cardiac Coronary Sinus. Heart, 1928, xiv, 241.

A case is recorded as an example of anatomical obstruction to the coronary circulation not on the arterial but on the venous side. The coronary sinus is occluded by a fibrous diaphragm apparently not due to a congenital malformation but to an old thrombus.

It would be thought that an obstruction in this situation if it did not cause death would interfere seriously with the coronary circulation but in the available history there is no unusual feature to suggest this nor was there any evidence in the heart itself of the impaired nutrition in the area drained by the occluded vein.

Grant, R. T., Wood, J. Edwin, Jr., and Jones, T. Duckett: Heart Valve Irregularities in Relation to Subacute Bacterial Endocarditis. Heart, 1928, xiv, 247.

From the point of view that subacute bacterial endocarditis arises through lodgement of bacteria on the valve surface a series of eighty-six hearts have been examined to note the irregularities present on the valves and to consider their possible relation to valvular infection.

The irregularities of the valve surface may be classified into two groups namely: recessions and projections. It is shown that neither recesses in the form of pockets and crevices nor projections in the form of connective tissue thickenings covered with endothelium can be regarded as offering bacteria a foothold on the valve.

It is found that small platelet thrombi occur with greatest frequency on those valves especially liable to subacute bacterial endocarditis. These thrombi are not themselves the result of bacterial invasion but are probably due to local secondary change in the thickened valves.

Such thrombi can be regarded as offering passing organisms a suitable foothold and nidus for their establishment.

It is suggested that if streptococcal invasion of the blood stream occurs at a time when a thrombus is forming on a heart valve then the conditions are suitable for the development of subacute bacterial endocarditis.

Kugel, M. A., and Epstein, Emanuel Z.: Lesions in the Pulmonary Artery and Valve Associated with Rheumatic Cardiac Disease. Arch. Path., 1928, vi, 247.

The present study was undertaken to determine the frequency and type of inflammatory changes in the pulmonary artery and valve and the adjacent fibrous ring in cases of rheumatic heart disease.

A systemmatical study was made in 24 cases of active rheumatic infection of the heart. In 5 of these histological examinations of the artery revealed an active inflammatory change consisting on the one hand of diffuse cellular infiltration in the intima and subintimal layers of the media and, on the other of a focal perivascular collection of cells comparable to the Aschoff nodules in the myocardium. These changes were similar to those described by Pappenheimer and von Glahn in the aorta. In two instances the intimal changes were sufficiently widespread to produce small macroscopic lesions on the inner surface of the vessel. In two cases the disruption of the elastic media was almost as conspicuous as in syphilis.

In fourteen of the active cases, the pulmonary valve was the seat of an interstitial valvulitis which involved a part of the whole of the valve, and in three of these the diffuse reactions was accompanied by the Aschoff bodies in the substance of the valve. Verrucae were present in six cases, but these were inconspicuous in all but two.

The musculo-arterial junction was the seat of active inflammation in seventeen of the twenty-four cases, or in 70.9 per cent. The more frequent type of reaction was of the diffuse variety, but Aschoff bodies were also present in a few.

In a comparative study of the aorta, its root and valves, the fibrous ring of this vessel which corresponds to the musculo-arterial junction of the pulmonary artery, was involved in twenty-two, or 90.7 per cent, of the twenty-four cases of active rheumatic heart disease. In four instances there were gross lesions in the intima, and these were more extensive in the aorta than in the pulmonary artery. Diffuse inflammatory changes were found in the wall of the artery in each of these cases. Aschoff bodies were not seen.

As controls, thirty-one cases of nonrheumatic pericarditis and seventy-five cases in which neither pericarditis nor rheumatic cardiac disease was present were studied. In one of the control cases lesions were found which could be confused with those seen in the pulmonary artery, valve and musculo-arterial junction in cases of active rheumatic cardiac disease.

Zinsser, Hans, and Yu, H.: The Bacteriology of Rheumatic Fever and the Allergic Hypothesis. Arch. Int. Med., 1928, lxii, 301.

The authors reported the cases described in this paper because they seemed to them to illustrate certain features in the bacteriology of rheumatic fever which were inconsistent with the assumption of a specific and single bacteriologic etiology in this disease. The cases were all of more or less the same clinical group; the organisms antigenically and in other respects differed from each other.

Moreover, the isolation of the bacteria in one case from the myocardium and in two—which illustrate the more chronic type of the disease—from the spleen, seems to offer a reasonable explanation for the frequent absence of these organisms from the blood stream and to point to the probable localization of the bacteria during the prolonged periods of quiescence. This also indicates the places

from which cultures at autopsy may be expected to yield the streptococci when they are absent from the blood and the pericardial exudate.

Moreover, a coordination of the observations in their cases with prolonged experimental studies on bacterial allergy seemed to them to lend added support to the point of view that focal infection with a consequent sensitization of the body is in keeping with the many otherwise contradictory experimental and clinical observations that have been made on this disease, and to lend added weight to the view that the allergic theory is a reasonable one as applied to the causation of many of the manifestations of rheumatic fever.

The authors have not yet been able in their experimental work to produce joint lesions in allergic animals except by direct injection of the antigen into the joints. All attempts to arouse sterile joint reactions in either allergic rabbits or guinea pigs by injecting the antigen intravenously or intraperitoneally have so far failed although they have been attempting this for a number of years. They have found that success in producing joint manifestations of any severity has usually necessitated repeated injections of the same joints.

The experimental circle of evidence, therefore, is not entirely closed, but it may be that in man the frequent association of joint manifestations with chilling, exposure, etc., may be due to the establishment thereby of abnormal circulatory communication between joints and the blood stream, in which sensitizing contact between the constituents of the blood stream and the joints can take place in a focally infected allergic person.

It seemed to them possible that the curious frequency with which nonhemolytic streptococci are associated with the disease, while at the same time nonhemolytic streptococci so found represent many varieties, may be due to the fact that with these organisms that peculiar balance between invasiveness and resistance is established in man, which most easily results in chronic infection.

At the same time, in appraising the significance of the different varieties of organism which Swift and his coworkers, as well as the authors, have found in one and the same case, it must be remembered that studies on bacterial mutation are considerably altering our opinions concerning the fixity of species; and modifications of the organisms inhabiting the body for months and years must be considered as possibilities until this chapter of bacteriology has made further progress.

The suggestion that many of the manifestations of rheumatic fever are dependent on the mechanism of bacterial hypersensitiveness is not a new one, but has been gaining force. On the whole, their observations of the last four or five years, both in the experimental study of bacterial allergy and in the analysis of clinical material, incline them to favor this view rather than that favored by Small, Birkhaug and others in which a single specific toxinforming organism is held responsible.

Kurtz, Chester M., and White, Paul D.: The Percussion of the Heart Borders and the Roentgen Ray Shadow of the Heart. A Study of One Hundred Cases. Amer. Jour. Med. Sc., 1928, clxxvi, 181.

The present paper is an endeavor to determine the trustworthiness of the percussion of the heart borders as compared with the "7 foot roentgen-ray plate."

The study is based on the examination of one hundred patients of all ages and both sexes seen in the out-patient department and wards of the Massachusetts General Hospital. The actual percussion was carefully done by three well trained observers and the roentgen-ray plates were measured and checked by a fourth.

Percussion is reasonably accurate as shown by comparison with a 7 foot roentgen-ray plate. It is simple, rapid and requires no apparatus and it is occasionally a valuable check on the accuracy of roentgen-ray technic and interpretation.

Percussion is of value in determining the cardiac outline especially in the third left interspace as this may be the only portion of the heart which is enlarged to physical examination, as in mitral stenosis and congenital heart disease. Percussion in the second interspace both to right and left and in the fourth right interspace should always be attempted because in case of marked increase widening can usually be detected even though the measurements themselves are bound to be inexact.

Hitchcock, C. H.: Studies on Indifferent Streptococci. 1. Separation of a Serological Group—Type I. Jour. Exp. Med., 1928, xlviii, 393.

Serological study of one hundred and fifty-nine strains of indifferent streptococci has revealed the existence of a large homogeneous group to which the designation Type I has been applied. All strains of Type I ferment inulin and salicin. The members of this type are not necessarily identical and further division into subtypes may be feasible.

Those strains not falling into the group of Type I are referred to as belonging to Group X. They are distinguished only by their failure to react strongly with Type I serum. The organisms of this group vary in their fermentive reactions with both inulin and salicin.

The organisms were secured from the throats of patients suffering from various diseases including rheumatic fever, from the throats of normal individuals, from the interior of tonsils removed at operation or from blood cultures of patients with acute rheumatic fever.

Hitchcock, C. H.: Studies on Indifferent Streptococci. II. Observations on the Distribution of Indifferent Streptococci in the Throats of Rheumatic and Non-Rheumatic Individuals. Jour. Exp. Med., 1928, xlviii, 403.

Indifferent streptococci occur in comparatively the same abundance in the throats of patients suffering from rheumatic fever or early in convalescence from the disease as they do in those who have recovered from the disease or in those of patients suffering from other diseases.

There is a slightly increased incidence of these microorganisms in the throats of hospital patients as compared with those of normal individuals.

Type I occurs with comparatively equal frequency and abundance in the throats of all four classes of individuals studied.

Cannell, D. E.: Myocardial Degenerations in Yellow Fever. Am. Jour. Path., 1928, iv, 431.

The microscopic examination and analysis of the hearts of twenty-nine cases of West African yellow fever and those of nine monkeys experimentally infected with West African yellow fever, is reported.

Cloudy swelling, granular and fatty degeneration were found constantly in the hearts of both the human cases and those experimentally induced in the monkeys.

Primary inflammatory changes were not seen in the hearts examined. Secondary response of white blood cells to intense degeneration was observed in two human cases.

The distribution and intensity of granular and fatty degeneration was patchy and variable. The lesions in the heart are in themselves not sufficient to make a diagnosis of yellow fever.

The causation of the slow pulse in yellow fever is still uncertain and doubt is thrown upon the belief that it is due to the jaundice.

Further investigation of the clinical function and the pathological changes in the bundle of His may lead to solution of this problem.

Johnson, Scott, and Siebert, Walter J.: Experimental Myocarditic Lesions in the Rabbit. Arch. Path., 1928, vi, 54.

The purpose of this study was to determine whether the heart of the rabbit in which myocarditis has been produced by the injection of caffeine and epinephrine is more susceptible to bacterial infection than the normal heart of the rabbit.

When rabbits so treated are subsequently injected intravenously with the bouillon culture of a suitable strain of staphylococcus aureus, abscesses of the heart are produced much more frequently than in rabbits not previously injected with caffeine and epinephrine. If a more active strain of staphylococcus is used, the abscesses occur even in the majority of the control animals. With this strain, also, the experimentally produced myocarditic lesion still influences the localization of the abscesses which develop in and around the myocarditic area mainly in the left ventricle and in the papillary muscles, and less frequently in the endocardium and in the left auricle.

Cardiac decompensation may be produced in rabbits by injection of caffeine and epinephrine alone as a result of the myocarditis thus produced; but the frequency of cardiac decompensation may be increased by subsequent injections of a suitable strain of staphylococcus aureus.

The proliferation of the endothelium which occurs adjacent to the myocardial lesion, following the injections of caffeine and epinephrine, appears to predispose the site of this lesion to the formation of mural thrombi in case a comparatively nonvirulent strain of staphylococcus aureus culture is injected into the blood stream subsequent to the injection of caffeine and epinephrine.

It was not possible to demonstrate any direct relationship between the acute vegetations on the valves of the heart and a lesion of the valves produced by the injections of caffeine and epinephrine.

The presence of a myocarditic lesion may indirectly favor the production of a fibrinous pericarditis and of pneumonia. On the other hand, injections of caffeine and epinephrine and the lesions produced thereby apparently do not markedly lower the resistance of the pericardium to the action of bacteria injected into the pericardial sac.

Bourne, C. R.: Auricular Flutter Restored to Normal Rhythm by Quinidine. Can. Med. Assn. Jour., 1928, xix, 180.

The interest in this report lies in the type of disturbance of cardiac mechanism and the method of its restoration to normal.

In a patient aged 38 there was an established auricular flutter in a heart definitely enlarged without gross cardiac failure. There was marked tolerance for quinidine and massive dosage was required to restore the normal mechanism of the heartbeat.

Digitalis improved the ventricular action, but apparently had a mild effect on the disappearance of the flutter.

Nathanson, M. H.: The Electrocardiogram in Diphtheria. Arch. Int. Med., 1928, xlii, 23.

In fifteen severe and moderately severe cases of diphtheria, approximately fifty per cent of the patients showed inversion of the T-wave in significant leads during convalescence.

Two patients showing inversion of the T-wave died suddenly.

In the patients that recovered, the inverted T-wave returned to normal as early as seven weeks after the onset of the disease.

Cats injected with sublethal doses of diphtheria toxin showed consistently similar T-wave alterations, usually within forty-eight hours.

These observations support the myocardial theory of the circulatory failure in diphtheria.

Barker, M. Herbert, and Levine, Samuel A.: Cardiazol: Some Experimental Effects of this Drug on the Cardiorespiratory Mechanism. Arch. Int. Med., 1928, xlii, 14.

In a series of experiments on cats it was found that cardiazol did not have any beneficial effect on the cardiorespiratory mechanism. This was true in the normal animal and in states of depression, produced by quinidine, hemorrhage and acid intoxication.

Miller, H. R., and Weiss, Morris M.: Disease of the Coronary Arteries. Arch. Int. Med., 1928, xlii, 74.

In cases of marked disease of the coronary vessels, together with a diseased heart on gross examination, the heart was found to be unhypertrophied and even small as revealed at autopsy in the nineteen cases tabulated in this study.

There were two patients with disease of the coronary arteries in whom clinical manifestations and roentgen-ray evidence pointed to cardiac enlargement. These hearts were dilated; they should not mistakenly be considered hypertrophied.

It may be that in the patients with disease of the coronary arteries in whom the heart remained small the organ failed to hypertrophy because it possessed a potential mechanism ready to function through adequate collateral channels whenever the coronary circulation was gradually blocked or impeded.

Carr, James H., and Reddick, Walter G.: Conduction Disturbances in Acute Rheumatic Infections. Jour. Am. Med. Assn., 1928, xci, 853.

This study covers fourteen cases of acute arthritis in which there was some disturbance of auriculo-ventricular conduction. This disturbance consisted of simple prolongation, incomplete block and complete block. The block was at times temporary.

In this group eight patients were taking sodium salicylate at the time the block was discovered and in no case was the drug stopped and in all the normal conduction time was restored while the same dosage was continued.

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Original Communications

THE TREATMENT OF RHEUMATIC CARDITIS BY ROENTGEN IRRADIATION OF THE HEART*

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INTRODUCTION

THERE are reasons for believing that roentgen rays, in suitable doses, might be expected to exercise an effect upon rheumatic lesions in the heart. Roentgen therapy has been successfully employed in the treatment of certain low grade infections, such as tuberculous lymphadenitis, acne, and iritis. Even more acute inflammatory conditions, such as carbuncles, furuncles, and erysipelas are often favorably influenced. The result of treatment appears to be a modification of the local tissue reaction, but the mechanism by which this is brought about is not understood.

Another effect of roentgen therapy is its effect upon scar tissue. Cicatrices of the skin become softer and more flexible after irradiation and keloids may be greatly reduced in size. In undertaking the present work, the treatment was at first given with the idea of modifying the character of the tissues in the region of the mitral valve in cases of mitral stenosis. In order to avoid any possibility of injury to the heart, small doses were used, comparable to those employed in the treatment of local infections. As it became apparent that changes were being induced in the myocardium with these quantities of irradiation, larger amounts were not employed. The amount of irradiation necesary to modify scar tissue is greater than such dosage and the time required for the change to occur is relatively long. It is probable, therefore, that this effect played no rôle in the results now reported.

LITERATURE

A detailed review of the literature concerning the effects of roentgen irradiation on the cardiovascular system was given in an earlier

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paper.[1] In summary, it has been shown that roentgen-ray therapy, though recommended for the relief of certain types of cardiac pain, is of doubtful value.[2] Post-mortem examination of the heart of one patient with Hodgkin's disease who received irradiation over the mediastinum showed myocardial lesions believed to denote specific roentgen-ray injury to the heart muscle.[3] In numerous other patients receiving roentgen therapy over the chest for various forms of thoracic tumor, and examined electrocardiographically and at necropsy, no evidence of cardiac damage was found.[4] In a series of rabbits irradiated over the heart with doses comparable to those employed in the clinic, transitory ventricular premature beats were recorded once. Pathologically, no characteristic changes were noted.[5] Following exposure of the right lung of dogs to considerably larger doses, cell necrosis, hemorrhage, and proliferation of connective tissue were found in the musculature of the right auricle.[6]

Since this abstract of previous work was compiled, three papers have appeared dealing with this subject. Tsuzuki[7] irradiated rabbits through the back. Thirty-six hours after exposure to 24 per cent of the skin erythema dose, he found fatty granules in the heart muscle cells. After 32 per cent of the erythema dose was given, the muscle cells showed beginning fatty degeneration; this was more distinct at the end of ninety-six hours. The author was uncertain whether the changes described were due to the direct or indirect effect of the rays.

Hartman and his collaborators[8] irradiated the anterior thoracic wall of dogs and sheep with from 3 to 18 times the human erythema dose given either in a single, massive exposure or in repeated smaller applications. Following such treatment they found gross and microscopic lesions in the heart muscle, and alterations in the electrocardiographic records. The graphic changes reported were inversion of the T-waves and the appearance of abnormal forms of T; cardiac irregularities, such as paroxysmal tachycardia, auricular flutter, and fibrillation; slight prolongation of the P-R interval; diminished voltage of QRS. It must be borne in mind that the amount of rays used was many times greater than is ever employed for clinical purposes. These authors also present the records of three patients who were given relatively large amounts of irradiation over the cardiac area incidental to treatment for mediastinal or lung tumors. Necropsy was performed in each instance and microscopic changes were described in the myocardium comparable to those found in the experimental animals. These reports do not present convincing evidence as to the relation between roentgen therapy and the changes observed in the heart. As stated by the authors, terminal infection in two cases and the advanced age of the third patient probably had a bearing on the findings.

Warthin and Pohle[9] exposed the precordium of rats and rabbits to a single dose of roentgen rays of short wave-length, the surface dose

being equivalent to one human erythema dose. No clinical symptoms of roentgen-ray injury were noted and there were no gross pathological changes at necropsy. In one out of twenty-four rabbits an unusual degree of Zenker's necrosis was found on microscopic examination. In two of thirty rats, hyaline degeneration was found in the heart muscle, of a degree warranting the conclusion that this change was caused by irradiation. It was concluded that a single exposure of the precordium of these animals to the dose described did not produce definite and irreparable injury to the heart.

MATERIAL AND METHOD OF STUDY

Two reports of our work have already been made.[1] In the present paper, further observations are included and a more detailed clinical analysis has been undertaken. Thirty patients with rheumatic carditis have received roentgen irradiation to the heart with the idea of attempting to influence the cardiac lesions of rheumatism in a favorable manner. In the group are included cases exhibiting various phases of rheumatic infection—acute and chronic, febrile and afebrile. There were patients in the first attack with early cardiac involvement; others had large hearts, severely damaged valves, and advanced mechanical defects. In seven cases, paroxysms of heart pain were a dominant feature. The material was intentionally varied in order to learn, if possible, which types of rheumatic heart disease might be affected by irradiation. In addition to noting changes in clinical condition, frequent electrocardiograms and numerous teleroentgenograms were made.

TECHNIC OF IRRADIATION

With the aid of a cross-section diagram of the chest at the level of the fourth chondrosternal junction and a depth-dose chart, there was calculated a quantity of rays yielding about 10 per cent of the erythema dose throughout the region of the heart. This was given in two fields, both front and back, large enough to include the entire cardiac area, each field being centered about 5 cm. to the left of the midline. It seemed advisable to use small doses in order to avoid any possible injury to the heart and because the quantity of rays used in the treatment of infections is not large.

The machine setting was: 200 KV (peak); 50 cm. target skin distance; 0.5 mm. copper plus 1.0 mm. aluminum filter. The usual dose was 36 milliampere minutes over the front and 54 to 72 milliampere minutes over the back, depending upon the size of the chest. If nausea and vomiting occurred, subsequent doses were decreased to 8 per cent of the calculated erythema dose. The treatment was repeated every two weeks until four had been given. At least a month was allowed to elapse before undertaking another series. The number of irradiations given to one patient ranged from two to twenty-five; most patients received at least one series of four. In this group of cases, it appeared likely that at least one series of four treatments was necessary to initiate improvement, when this occurred. More prolonged therapy is probably desirable. Modification of the technic may yield better results.

RESULTS

Changes in the Electrocardiogram.—In normal individuals, the form of the electrocardiogram remains quite constant over long periods of time. As a result of disease of the heart, changes may occur. In rheumatic fever, electrocardiographic evidence of myocardial involvement, as shown by alterations in the form of the graphs, is frequently obtainable.[10] These changes are not to be regarded as specific for rheumatism; they are merely an expession of disturbance in the heart muscle. In this study, several control records were always made and the effect of digitalis was excluded. Except for occasional shortening of A-V conduction time,[11] salicylates, in our experience, do not modify the electrocardiogram in rheumatic fever. It is believed that the changes observed in our cases were due to the effect of irradiation on rheumatic lesions in the heart muscle. The fact that changes in the form of the graphs did not occur in every instance lends support to the concept; for myocardial lesions are not found in every case of rheumatic heart disease. Furthermore, it seems probable that the lesions vary in their susceptibility to the effects of irradiation at different stages of their evolution. It is impossible at present to form an opinion concerning the possible effect of the rays on valvular lesions.

TABLE I

SUMMARY	
30 Cases	
249 Roentgen Irradiations	
649 Electrocardiograms	
DURATION OF FOLLOW-UP SINCE FIRST IRRADIATION	
3 years	3 cases
2 to 3 years	4 cases
1 to 2 years	9 cases
Less than 1 year	14 cases
ELECTROCARDIOGRAPHIC CHANGES	
Present	17 cases
Absent	13 cases
CLINICAL CONDITION	
Improved at the End of the Follow-Up Period	21 cases
Improved Temporarily	3 cases
Unimproved	1 case
Died	5 cases
RELATIONSHIP OF ELECTROCARDIOGRAPHIC CHANGES TO CLINICAL CONDITION	
Improvement with EKG. Changes	14 cases
Improvement without EKG. Changes	10 cases
EKG. Changes without Improvement	3 cases
Neither Improvement nor EKG. Changes	3 cases

Changes in the form of the electrocardiogram were observed in 17 of the 30 cases. In 14 of these 17 cases, clinical improvement was also noted. But clinical improvement was noted also in 10 cases in which no graphic changes were recorded. It appears, then, that change in clinical condition and change in the electrocardiogram do not necessarily parallel each other; but following irradiation, electrocardiographic change without betterment is uncommon.

The alterations in the form of the curves were of numerous varieties:

a. Inversion or deepening of the T-waves—18 cases. This was the change most frequently observed. It was seen sometimes in all leads, but occasionally only in Lead III. In Fig. 1 is shown an example of this effect. Slight deepening of the T-wave in Lead III is seen on the day following the first exposure (May 28). Six weeks after beginning roentgenotherapy, and after the fourth treatment, T_3 is seen to be sharply inverted and T_2 distinctly flattened (July 9). Treatments were then discontinued. By December 29, some five months later, T_3 was upright and T_2 higher. Following a second series of roentgen-ray exposures, the T-waves again showed changes similar to those seen after the first series, though of somewhat less marked degree. The same sequence of events was repeated a third time. In this case, clinical improvement was striking.

b. Inversion or flattening of the P-wave—9 cases. This was seen as a transitory change, appearing usually soon after beginning roentgenotherapy and, as in the case of the T-wave changes, sometimes recurring after successive courses.

c. Change in electrical axis—7 cases. This was an interesting finding. It is a change which we have observed also in cases of rheumatic heart disease with active myocardial lesions, uninfluenced by roentgenotherapy. The shift was always in the direction of right axis deviation. (Fig. 2.)

d. Change in the form of QRS—5 cases. Variations in the position and shape of the notch in R or S, as well as differences in the duration of QRS were noted. In the example pictured in Fig. 3, changes in the form and direction of P and T are also shown.

e. Ventricular premature beats—3 cases. These occurred within a day or two after exposure and suggested the possibility of an irritative reaction in the myocardium (Fig. 1).

f. Auricular premature beats—2 cases. These probably have the same significance as the extrasystoles of ventricular origin.

g. Elevation or depression of the R-T interval—2 cases. Like the other changes, this denotes disturbance in the myocardium.

h. Shortening of auriculo-ventricular conduction time—1 case. (See Table II.)

TABLE II

L. V., MALE, AGED SIXTEEN. PRESBYTERIAN HOSPITAL NO. 64000

DATE	RADIO-THERAPY	EKG. DATA						ATTACKS OF PAIN IN 24 HR.	HIGHEST TEMP.	SALICYLATE (GM.) DAILY	LEUCOCYTES	REMARKS
		RATE	P-R (SECS.)	T-WAVE			QRS CHANGE					
				I	II	III						
1925												
Oct. 5		83	0.24	–	+	+			100.4			
Oct. 14		100	0.38+	–	+	+			99.0	2.4	16,000	Admitted Oct. 4
Oct. 16		75	0.29	–	+	+			99.0	2.4	14,200	In bed
Oct. 18								12	99.0	2.4		
Oct. 20		78	0.28	–	+	+		11	99.0	2.4	11,800	
Oct. 23		71	0.37	–	+	+		8	99.0	3.6		
Oct. 27		75	0.25	–	+	+		10	99.0	3.6	11,800	
Nov. 7								9	99.8	3.6	11,500	
Nov. 10		68	0.37	–	+	+		4	99.1	4.8	10,700	
Nov. 17		68	0.37	–	+	+		8	99.6	3.6		
Nov. 24		68	0.38	–	+	+		10	99.8	0.0		
Nov. 30	I							8	99.6	3.6		
Dec. 5								14	98.8	3.6		
Dec. 7	II							12	98.8	3.6		
Dec. 8								1	98.8	3.6	10,000	In chair
Dec. 14		88	0.38	–	+	+		0	99.2	0.0	7,500	
Dec. 15	III							0	98.6	0.0		
Dec. 20								0	102.2	0.0	15,500	Splenic infarct
Dec. 23	IV	78	0.20	–	+	+	+	2	100.6	0.0		
Dec. 28								2	99.6	1.2	10,000	
Dec. 31		102	0.19	–	+	+		0	99.0	2.4		

TABLE II—CONT'D

DATE	RADIO-THERAPY	EKG. DATA RATE	P-R (SECS.)	T-WAVE I	II	III	QRS CHANGE	ATTACKS OF PAIN IN 24 HR.	HIGHEST TEMP.	SALICYLATE (GM.) DAILY	LEUCOCYTES	REMARKS
1926												
Jan. 4								1	99.0	1.2	7,000	
Jan. 12		71	0.24	−	+	+		2	99.0	2.4	11,000	
Jan. 19	V							1	99.0	2.4	7,500	
Jan. 21		50	0.24	−	+	+	+	1	98.8	2.4		
Jan. 26		68	0.25	−	−	+	++	1	99.4	2.4	8,000	
Jan. 27	VI	78	0.36	−	−	+	+	2	98.8	2.4		
Jan. 28		70	0.30	−	−	+	+	2	98.4	0.0		
Jan. 29		83	0.18	−	+	+	++	0	98.8	0.0		
Jan. 30		94	0.19	−	+	+		1	99.0	0.0		
Feb. 1		100	0.18	−	+	+	+	1	100.6	0.0		Splenic infarct
Feb. 2	VII	85	0.20	−	+	+		1	101.6	0.0		
Feb. 3		93	0.18	−	+	+		0	100.8	0.0		
Feb. 4		85	0.17	−	±	+	+	0	101.0	0.0		
Feb. 5		83	0.19	−	+	+	+	1	100.6	0.0	11,000	
Feb. 6		78	0.20	−	+	+		1	99.8	0.0		
Feb. 8		78	0.20	±	+	+		0	99.6	0.0	13,000	
Feb. 9	VIII							0	99.4	0.0		
Feb. 10		88	0.18	−	±	+	++	0	99.2	0.0		
Feb. 12		88	0.20	−	+	+	++	1	99.4	0.0		
Feb. 13		88	0.20	−	+	+		1	99.2	0.0		
Feb. 16		79	0.20	−	±	+	++	0	99.0	0.0		
Feb. 17		78	0.20	−	+	+	+	1	98.6	0.0		
Feb. 19								1	99.2	0.0	7,000	
Feb. 23		83	0.20	−	+	+		1	99.6	0.0		

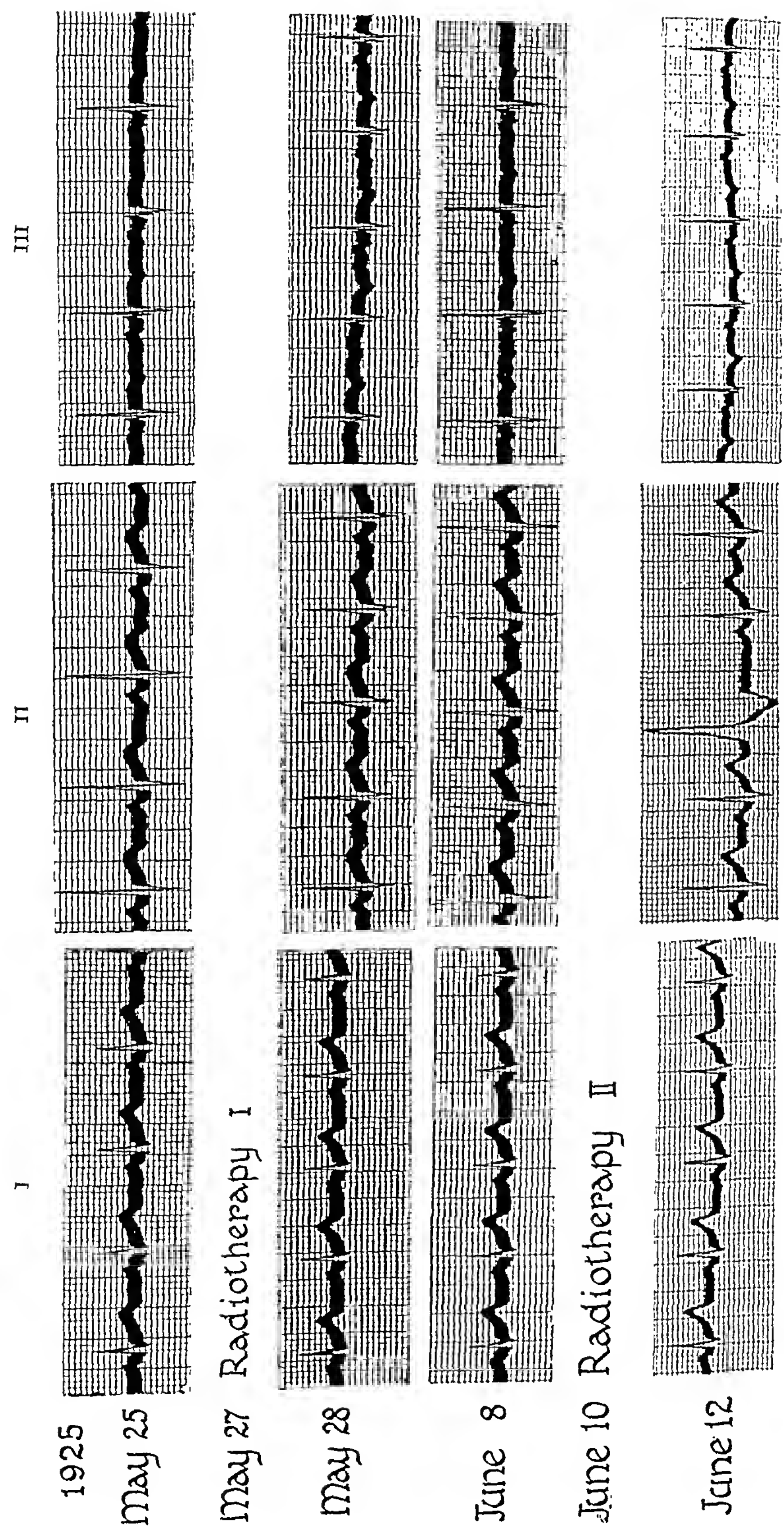
I
II
III
1925
May 25
May 27 Radiotherapy I
May 28
June 8
June 10 Radiotherapy II
June 12

Fig. 1.

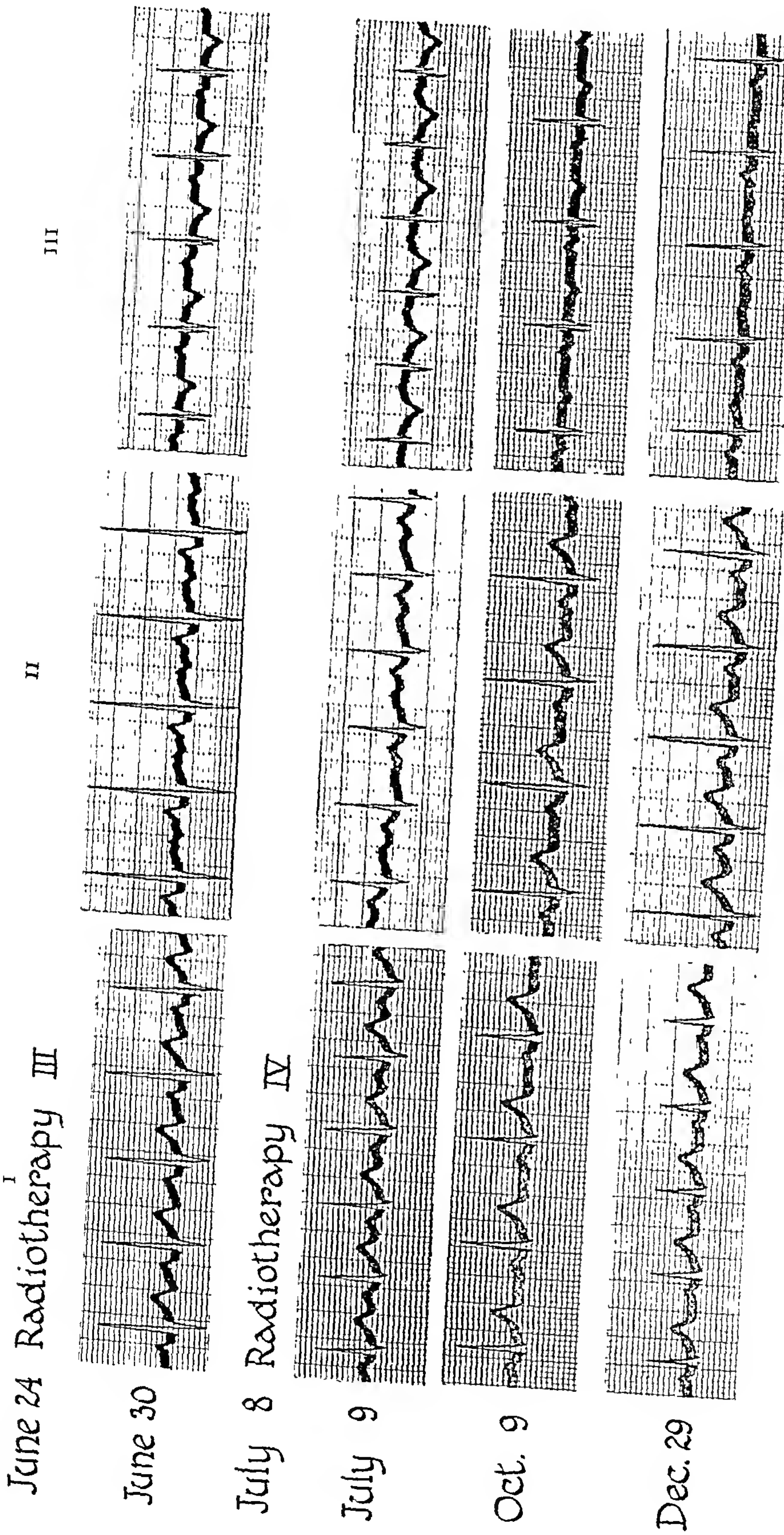

Fig. 1. (Continued.)

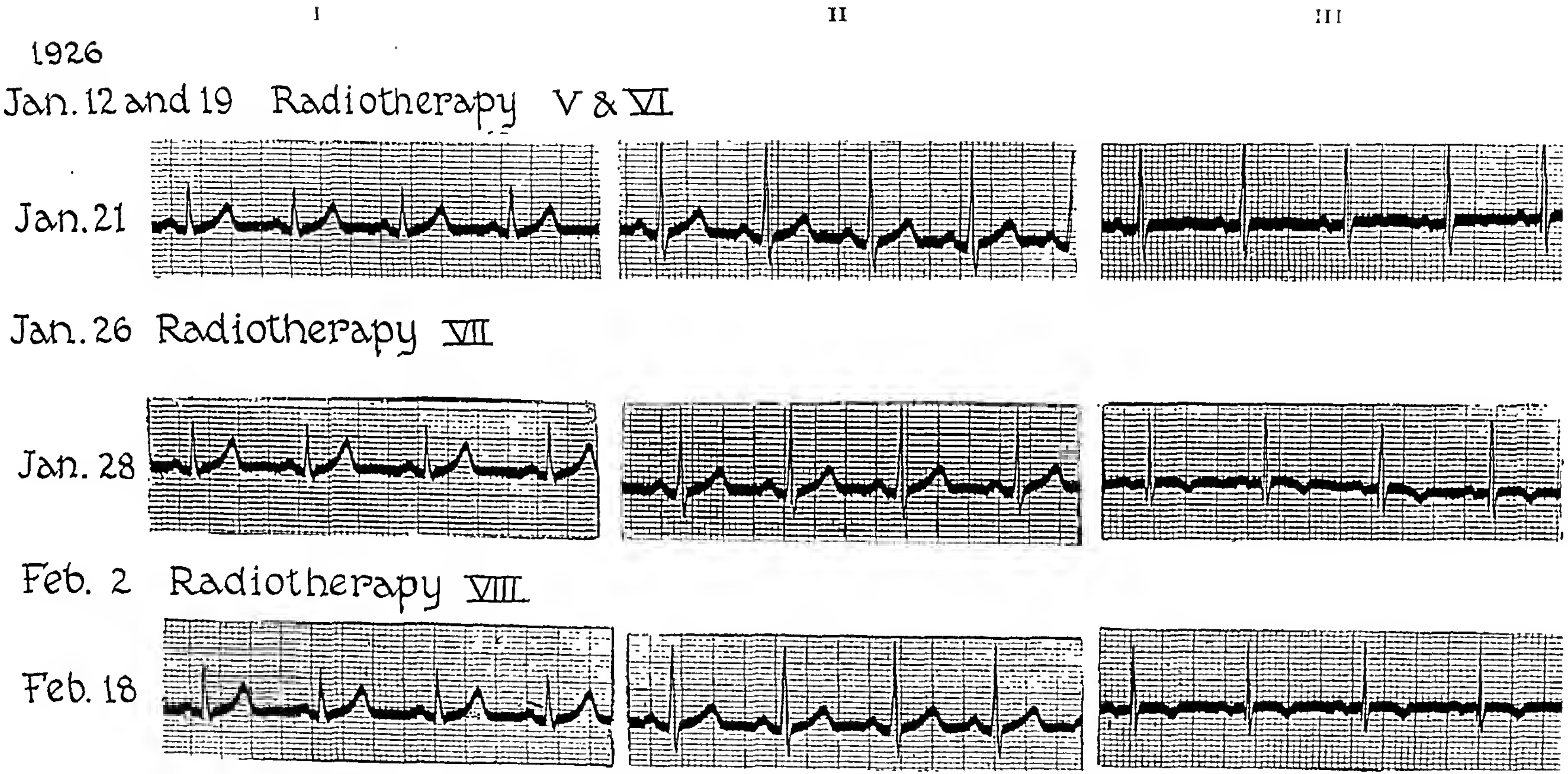

Fig. 1.—Effect of irradiation on the T-wave of the electrocardiogram. The record of May 25 serves as control. Following irradiation, the T-wave in Lead II becomes progressively flatter, in Lead III it becomes sharply inverted. The effect is most marked in the record of July 9. From July 22 to December 29, no roentgenotherapy was given. The record taken on the latter date shows a return of the T-waves to the forms observed in the control. Following a second course of irradiation, begun on January 12, the T-wave in Leads II and III undergoes changes similar to those seen after the first course, though of less marked degree. The same cycle of events was repeated a third time.

In the record of June 12 is seen a ventricular premature beat, occurring two days after the second roentgenotherapy.

The time of appearance and duration of the form changes in relation to irradiation were variable. As stated, T-wave inversion usually began soon after beginning treatment, progressed gradually, and lasted often for weeks or months. Alterations in QRS were sometimes temporary, but were occasionally permanent, as shown in Fig. 3. The

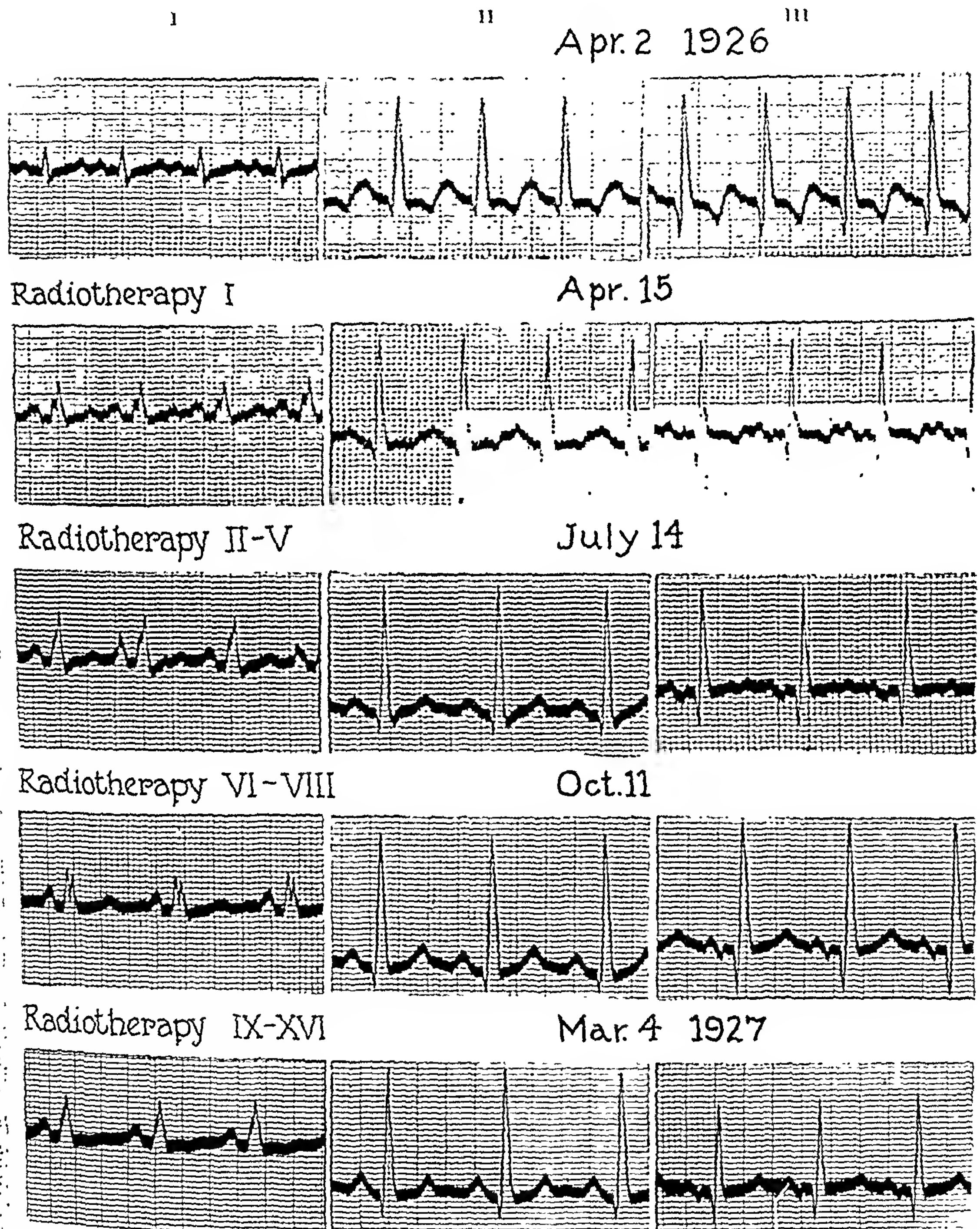

Fig. 2.—Effect of irradiation on the QRS group of the electrocardiogram. The changes are most marked in Lead I. The R-wave becomes sharply notched following irradiation and the notch changes its form and position in successive graphs.

The record also shows alterations in the P- and T-waves in Leads II and III. After showing changes continuously over a period of sixteen months, the form of the curves became constant and has remained so for eight months.

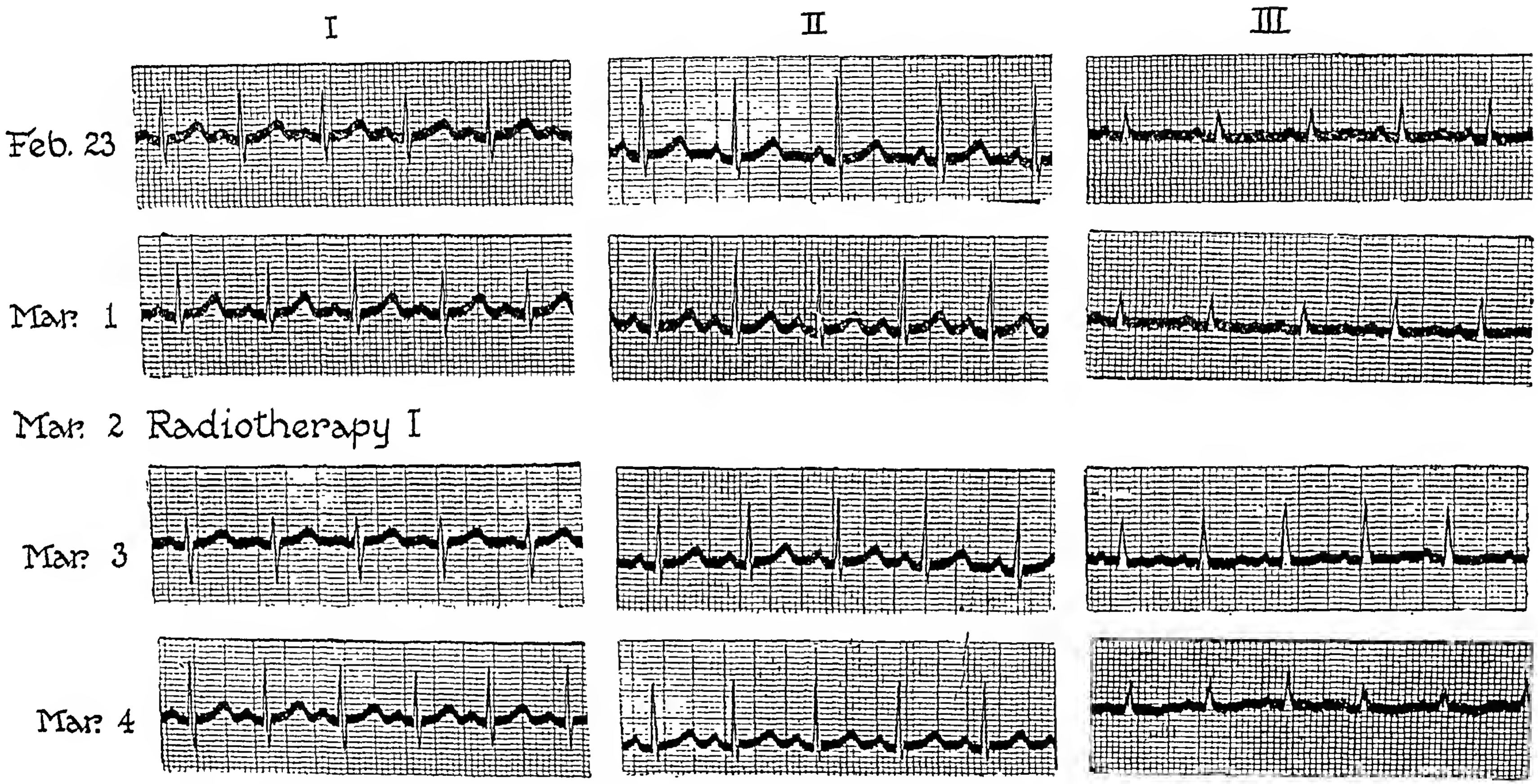

Fig. 3.—Effect of irradiation on the electrical axis. Two control records are shown, taken one week apart. Following irradiation, there is a shift of the electrical axis to the right, resulting in the sequence known as right ventricular preponderance. The change *is* transitory, and two days after irradiation, the graphs resemble those seen in the controls.

other changes appeared soon after an exposure and were evanescent, disappearing often in the course of a few days.

Effect on Clinical Conditions.—Because cases of varying degrees of severity were included in the group, representing different stages of rheumatic infection, it was to be expected that the results would be variable. It is also possible that some of the patients did not receive a sufficient number of treatments. Of the thirty patients, twenty-one (70 per cent) were considered improved at the end of the follow-up period. Variability and uncertainty in the clinical course of rheumatic fever are well known. To propose to establish the value of a therapeutic procedure on the basis of a small series of cases, however carefully observed, is clearly unsound. It is our impression that in many of these cases, improvement was definitely related to roentgenotherapy. The change in condition was evidenced by cessation of fever, fall in heart rate, disappearance of leucocytosis, and gain in weight. In most of the cases, salicylates and drugs of the cinchophen group were given. Where possible, a control period, free from all other therapy, was carried out prior to starting irradiation. The five patients who died had advanced lesions and continuously active rheumatism with progressive myocardial failure. Some of the instances of improvement were striking. Seven patients had paroxysms of severe cardiac pain. Five of these were relieved during the follow-up period. The results can best be indicated by citing briefly a few illustrative cases, including both favorable and unsuccessful examples.

CASE 1.—A girl of thirteen years gave a history of recurring arthritis for four years, with dyspnea and edema for nine months. The heart was large and showed a double mitral lesion. She had been in the hospital for nine months, during which there was continued fever, tachycardia, chest pain, and leucocytosis, although the joint manifestations were negligible. Salicylate and neocinchophen were administered repeatedly in large doses, and several small transfusions were given. Heart failure was controlled with digitalis. All discoverable foci of infection were carefully eradicated. Low grade infection persisted and appeared to be chiefly in the heart. Five days after the first irradiation, the temperature fell to normal, with parallel decrease in heart rate. With but few minor setbacks improvement continued. During the next eleven months she received thirteen roentgen treatments. Following roentgenotherapy, the electrocardiograms showed a striking shift in electrical axis on two occasions, and slight changes in P, T, and the R-T interval at other times. Auricular premature beats were noted once. It is now over three years since radiotherapy was begun, and she has had none for over two years. The electrocardiogram has been constant in form for eighteen months. There has been no recrudescence, she has grown and gained weight, and goes to public school. The relationship between irradiation and the onset of improvement seemed definite; and the course since leaving the hospital has been much more favorable than might have been anticipated in this type of case.

CASE 2.—A boy of sixteen years, with enormous heart, double mitral lesion, and aortic insufficiency, had had recurring rheumatic infection since the age of twelve. Heart symptoms appeared at the age of thirteen. Tonsillectomy was performed

at the age of ten. For three years he had been bedridden, suffering from severe paroxysms of heart pain. During these attacks his blood pressure would often rise to above 200 mm. Hg. and he would break out in a cold perspiration. Nitroglycerin afforded relief. At the time of admission to the hospital, he was having as many as twelve of these paroxysms in the course of twenty-four hours and was taking up to 20 tablets of nitroglycerin daily. There was slight fever. The leucocytes were 16,000. The electrocardiogram showed sinus rhythm, marked left ventricular preponderance, prolonged P-R interval, inversion of T_1 and notching of R_2. Clearly, there was marked myocardial damage with active lesions present in the heart muscle. His course and response to irradiation are shown in Table II. Of greatest interest is the relief from paroxysms of pain. Conduction time (P-R interval) returned to within normal limits. Fever and leucocytosis likewise subsided except when embolic infarction of the spleen occurred on two occasions. The electrocardiogram, constant in form prior to beginning roentgenotherapy, began to show changes after the third treatment, shortly after the onset of clinical improvement. Salicylate was given only in small doses because it was poorly tolerated; it seems improbable that it played a rôle in the relief of pain.

Unhappily, the attacks of pain recurred after four months of relative comfort. Left cervical sympathectomy was then done under local anesthesia. The boy died three days later of myocardial failure. Necropsy was not permitted.

Case 3.—A girl of eighteen years (a private patient of Dr. D. W. Atchley), had rheumatic fever annually from the ages of seven to fourteen, and again at seventeen. She was admitted to the hospital complaining of slight arthritis, dyspnea, and paroxysms of severe heart pain, with radiation to the left arm. Dyspnea had been present for one year, the pain for one month. The heart was greatly enlarged. There were signs of mitral stenosis and insufficiency but no aortic valve lesion was made out. During a period of seventeen months twenty-five irradiations to the heart were given. The form of the electrocardiogram changed frequently during the first sixteen months, then became constant and has remained so for eight months. The attacks of precordial pain have entirely disappeared, the functional capacity of the heart has improved, and the patient is working in a secretarial position. In this case, complete relief from pain was afforded and a smouldering carditis was apparently converted into an inactive myocardial fibrosis.

Case 4.—A colored girl of eleven years had her first attack of chorea and arthritis two years before entering the hospital. Tonsillectomy was performed shortly after admission. Fever was continuous, though not high; the heart was large, with double mitral lesion. Numerous subcutaneous nodules were present. Five irradiations were given during a period of three months. There was slight flattening of the T-waves in Leads II and III, and transitory right preponderance appeared after the third treatment. Although constantly in bed, heart failure and signs of a tricuspid lesion developed. New crops of nodules appeared from time to time and leucocytosis was persistent. She died ten months after the first roentgenotherapy, with all the evidences of progressive, active rheumatism and with myocardial failure. Necropsy was not performed. In this case, a severe rheumatic infection was entirely uninfluenced by roentgen irradiation of the heart.

In view of these experiences, what conclusions may be drawn as to the type of patient most suitable for roentgenotherapy? Early cases, in the first attack, with beginning cardiac involvement obviously offer the best material. More advanced cases, with paroxysmal heart pain, have been afforded relief in five of seven cases. In a number of cases

of low-grade infection with predominantly cardiac involvement, it appeared that the infection subsided. Patients with advanced mechanical defects and outspoken cardiac failure, as well as those with signs of overwhelming rheumatic infection, have proved unsuitable subjects.

Effect of Roentgen-ray Therapy on Heart Size.—No changes were observed in the teleroentgenograms which could be related to irradiation. Particular mention is made of this point because Beeck and Hirsch[2] described diminution in the width of the aorta in one of their cases, after irradiation.

TABLE III

UNPLEASANT EFFECTS IN 30 PATIENTS RECEIVING IRRADIATION OVER THE CARDIAC AREA

Nausea and vomiting	8 cases
Increased chest pain	3 cases
Headache	2 cases
Exacerbation of fever	1 case

Unpleasant Effects.—In no instance was there evidence that the heart was injured or the course of the disease unfavorably influenced. Fourteen patients had mildly unpleasant effects which are shown in Table III. Nausea, vomiting, and headache are familiar radiation reactions. Increased chest pain and fever may, perhaps, be attributed to a disturbance induced in specific rheumatic lesions.

EFFECT OF IRRADIATION OF THE HEART IN SUBACUTE BACTERIAL ENDOCARDITIS

A limited number of irradiations were given to four patients with nonhemolytic streptococcus endocarditis. Three of the patients received three treatments, the fourth patient only two. There was no demonstrable effect either on the electrocardiograms or on the fatal progress of the disease. All of the patients died within three months. One patient, who received two irradiations, came to necropsy. No changes were found in the heart which could be ascribed to irradiation.

POSSIBLE MODE OF ACTION OF IRRADIATION ON THE RHEUMATIC HEART

As the result of therapeutic experience with various forms of local infection, as stated in an earlier paragraph, it appears that roentgen irradiation modifies the tissue response to the infection in a manner favorable to recovery. In this connection the experiments of Bass[12] are suggestive. He injected rabbits intravenously with a culture of virulent streptococci. Animals irradiated over the abdomen with 50 per cent of the skin erythema dose of x-rays lived from five to ten days, whereas nonirradiated animals died in from one to three days. The action of the rays, in Bass' opinion, is general as well as local, and is probably brought about through activation of the reticulo-endothelium by cellular decomposition products.

Renewed interest in the rôle of allergy in rheumatic fever has been stimulated by the recent work of Swift and his collaborators.[13] They have formulated the hypothesis that in this disease the tissues of the body have become allergic to the products of certain nonhemolytic streptococci, the allergizing substance being produced in a focus such as the tonsils. Sensitization is not necessarily specific for any particular variety of streptococcus.

It has been shown that radiant energy (ultraviolet light) modifies the reaction of the skin to certain bacterial products when these are injected into it. Thus, the intradermal tuberculin test in guinea pigs and patients gives a lessened reaction when the injected area is treated locally with short exposures of ultraviolet rays, either before or after injection.[14] Such a phenomenon may be interpreted as indicating a process of desensitization. Is it not conceivable that in rheumatic fever roentgen irradiation serves to desensitize the tissues of the heart to an allergizing substance, thereby favoring the subsidence of existing lesions and, for a time at least, preventing further cardiac damage? The action of the rays may be local, or general, or perhaps both.*

CONCLUSION

Cardiac involvement constitutes the chief menace in rheumatic fever. As yet, neither the causative agent of the disease nor a specific remedy for it are at hand. In certain cases of rheumatic carditis, roentgen irradiation of the heart appears to exert a favorable influence. It is possible that in patients having their first attack of rheumatism, with or without evidence of cardiac involvement, irradiation may be useful in minimizing the danger of damage to the heart.

SUMMARY

1. Thirty patients with rheumatic heart disease were given 249 roentgen irradiations over the cardiac area. The machine setting was calculated to yield about 10 per cent of the erythema dose distributed throughout the heart muscle. In addition to noting changes in clinical condition, frequent electrocardiograms and numerous teleroentgenograms were made.

2. Following irradiation, changes in the form of the electrocardiogram were observed in 17 of the 30 cases. It is believed that these changes were due to the effect of irradiation on the myocardium, with modification of the rheumatic lesions.

3. Of the 30 cases, 21 (70 per cent) showed clinical improvement at the end of the follow-up period. Three improved temporarily, 1 was

*Since this article was prepared for publication, Zinsser and Yu (*Arch. Int. Med.*, 1928, xlii, 301) have adduced evidence which lends support to the view that focal infection, with consequent sensitization of the body, is the cause of many of the manifestations of rheumatic fever. They have isolated streptococci from the myocardium in one case and from the spleen in two cases at necropsy, and suggest that these foci may represent the localization of the bacteria during periods of quiescence.

unimproved, and 5 died. Those cases terminating fatally were all instances of continuously active rheumatism, with advanced lesions and progressive cardiac failure.

4. In 5 of 7 patients with paroxysms of severe heart pain, relief from this symptom followed roentgenotherapy.

5. Early cases, in the first attack of rheumatic fever, offer the best chance for success in therapy. In a number of cases with low-grade infection, predominantly cardiac, it appeared that the infection subsided following roentgenotherapy. It seems likely that at least one series of four treatments is necessary to initiate improvement. More prolonged therapy is probably desirable.

6. No changes were observed in the teleroentgenograms which could be ascribed to the effects of irradiation.

7. Unpleasant symptoms were noted in 14 cases. These were due, for the most part, to radiation reactions. In no instance was there evidence of injury to the heart or an unfavorable effect on the course of the disease.

8. In 4 cases of subacute bacterial endocarditis due to nonhemolytic streptococcus, roentgen irradiation of the heart caused no change in the form of the electrocardiogram, nor did it arrest the fatal progress of the disease.

9. It is suggested that in rheumatic fever, roentgen irradiation of the heart may serve to desensitize the tissues of the heart to an allergizing substance, thereby favoring the subsidence of existing lesions and preventing further cardiac damage.

10. In patients having their first attack of rheumatism, irradiation may be useful in minimizing the danger of damage to the heart.

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OBSERVATIONS ON CERTAIN ETIOLOGICAL FACTORS IN RHEUMATISM*

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THE importance of acute rheumatic fever and its accompanying condition, rheumatic heart disease, is being increasingly recognized as a public health problem. Efforts are constantly in progress to form a true picture of the disease from the standpoints of epidemiology, infectivity, communicability, and bacteriology. This study is offered, not for any definite conclusions which can be drawn, but to present certain facts which may be added to other facts, and in the final analysis give us accurate knowledge of rheumatism and its natural history.

The term "rheumatism" used in this paper refers to chorea and acute rheumatic fever. The material was drawn from the Children's Medical Service of Bellevue Hospital in New York City, both ward cases and cases from the Huddleston Memorial Cardiac Class. The cases from the wards include all admissions for rheumatism in the years 1923 to 1927, and were not selected in any sense. The records of about 2000 cases which had gone through the cardiac class were reviewed, and accurate data found on about 500 of these. The patients were children up to the age of thirteen years. The points considered were: (1) race, (2) sex, (3) age at onset of rheumatism, and (4) seasonal incidence.

Table I

Race	Per cent in cardiac class	Per cent in general pediatric clinic
Italian	23.5	19.56
Jewish	21.94	27.4
American	19.00	14.48
Irish	15.8	4.3
German	5.33	4.1
Polish	3.95	3.7
Hungarian	2.76	1.17
Austrian	1.58	4.7
English	1.38	0
Spanish	1.18	5.09
Greek	0.98	3.3
Czecho-Slav	0.98	1.6
Colored	0.59	1.6
Finn	0.19	0
Ukranian	0.19	0
Armenian	0	5.47
Roumanian	0	2.34

*From the College of Physicians and Surgeons, Columbia University, and the Childrens' Medical Service, Bellevue Hospital and the Huddleston Memorial Cardiac Class.

RACE

It is well known that rheumatism and rheumatic heart disease are common in certain countries; namely, Great Britain, North America, and Germany, while certain races, such as the Chinese, Japanese and natives of India are seldom affected. This suggests the possibility that climate may be a factor in the incidence of these conditions, but this is difficult to determine conclusively. Racial susceptibility must be considered as a possible factor, but here also it is difficult to draw fixed conclusions in the absence of a very large number of cases. If we can show that a certain racial stock in this country has a high incidence, while in its own country it has a low incidence, it is reasonable to believe that climate is more of a factor than race.

Table I shows an analysis by race of 506 children in the cardiac clinic at Bellevue compared with the race of 511 children in the general pediatric clinic. This demonstrates that although the Italians form only 19.56 per cent of the population of the general clinic, they comprise 23.5 per cent of the cardiac class. Similarly, 27.4 per cent of the children in the general clinic are Jewish, while only 21.94 per cent of the cardiacs are of this race. This suggests that the Italians in New York City are somewhat more susceptible to rheumatic heart disease than are the Jews of this city. A more striking comparison is shown in the figures for the Irish. Of the cardiac patients, 15.8 per cent are Irish, although only 4.13 per cent of the patients in the general clinic are of this race. The Irish in Ireland do not have a high rate for heart disease. Again, while there were no English among the sample from the general clinic, 1.38 per cent of the cardiac patients were English. Native born Americans form 14 per cent of the general clinic and 19 per cent of the cardiac clinic. The type of population of the neighborhood in which a clinic is located may affect the races which attend the clinic, but Bellevue, which is a municipal hospital, draws its patients from all parts of the city as well as nearby suburbs, so that this factor does not operate as it would in a strictly neighborhood clinic.

These findings suggest that in New York City certain races are more susceptible to rheumatism and rheumatic heart disease than certain other races, and that climate may be a factor.

SEX

Females are slightly more frequently affected with rheumatic heart disease and rheumatism than males. Of the 506 cardiac children from the out-patient department, 214 were boys and 292 were girls. The combined percentages for Bellevue and one other smaller clinic were, boys 44 per cent, girls 56 per cent.

AGE AT ONSET

The figures for this part of the study apply only to cases where a definite date could be obtained for the first attack of chorea or acute rheumatic fever. No attempt was made to include cases where the first rheumatic manifestation was an endocarditis.

Fig. 1 shows the curve for 623 cases of both sexes. The peak of this curve occurs at nine years. When the sexes are separated, a rather interesting fact is disclosed: namely, that the peak for the boys comes two years earlier (i.e., at seven years) than the peak for

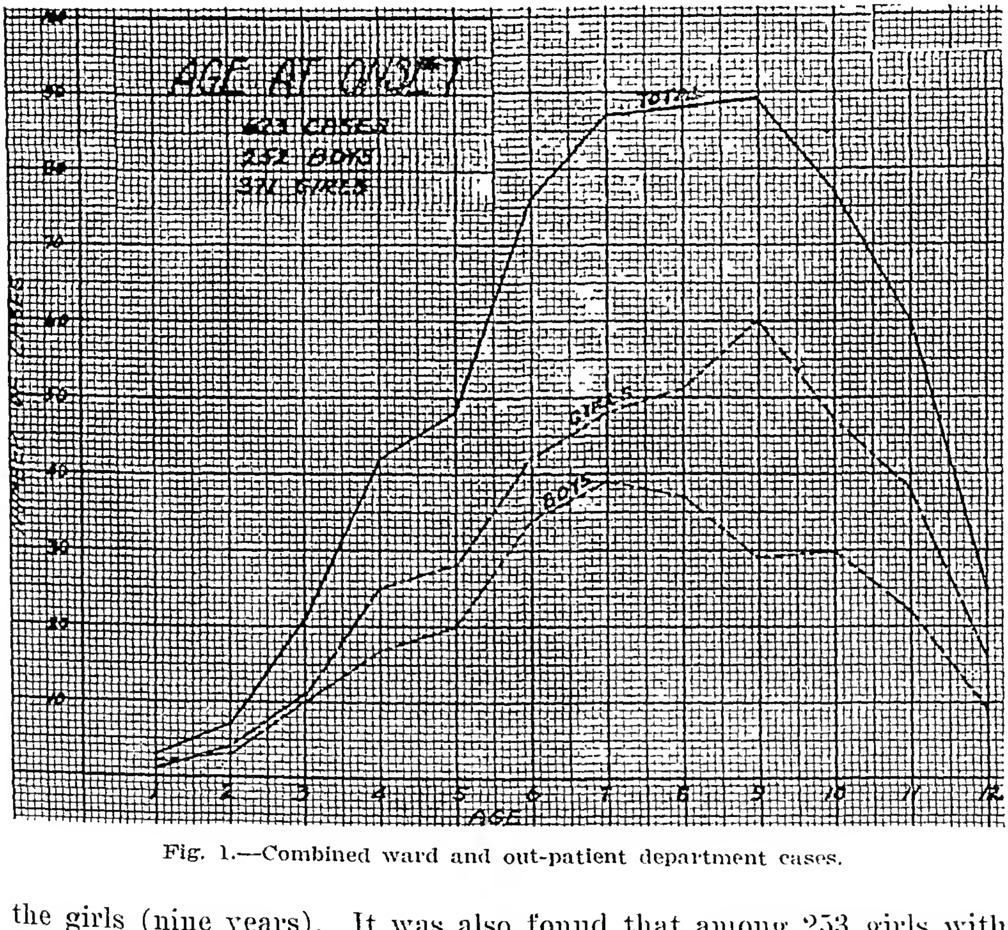

Fig. 1.—Combined ward and out-patient department cases.

the girls (nine years). It was also found that among 253 girls with rheumatic heart disease 21 per cent gave no history of chorea, acute rheumatic fever, or growing pains prior to the discovery of heart disease, and that of 174 boys, 14 per cent gave no such history. Since we know that a greater number of girls than boys develops rheumatic heart disease, this suggests that girls have an inherently greater susceptibility, so that an infection which is not sufficiently overwhelming to produce an attack of acute rheumatic fever may give an endocarditis without marked symptoms. To state it in another way, rheumatism more frequently manifests itself in girls primarily as an endocarditis than it does in boys.

SEASONAL INCIDENCE

As had been expected, a definite seasonal incidence for rheumatism was found. The greatest number of attacks begins in April, the next greatest in May. This does not coincide with the findings in Great Britain.[1] Fig. 2 gives the curve for 584 cases of chorea and acute rheumatic fever according to the month in which the attacks began. The data were taken from the hospital cases from 1923 to 1927 (389 cases) plus the out-patient department cases, which were not selected by years. Since the curves made for these two samples separately were seen to be similar, the figures were combined to make a single

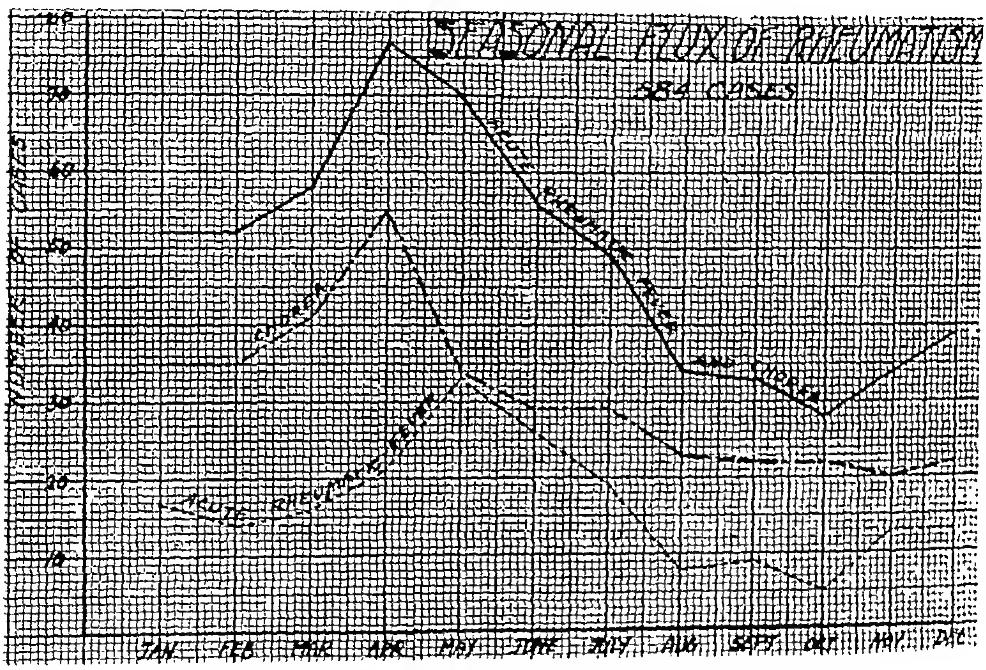

Fig. 2.—Combined ward and out-patient department cases.

curve. In this same figure the curves for chorea and acute rheumatic fever are separated. There is a lag of acute rheumatic fever compared with the curve for chorea, i.e., the peak of the curve for chorea occurs in April, and the peak for acute rheumatic fever in May.

In Fig. 3 are compared the findings from 459 cases taken from two hospitals in London and one in Glasgow,[1] and the 584 cases from Bellevue Hospital. The British figures show that 12 per cent of their cases occurred in November and 11 per cent in January, while June and July had the lowest percentage, namely, 5 per cent. In contrast to this the New York figures show that 13 per cent of the cases occurred in April, and 12 per cent in May, with October as the low month with 5 per cent.

METEOROLOGICAL CONDITIONS

It was thought that the difference in seasonal incidence of rheumatism found in London and Glasgow, and in New York, might be explained by meteorological conditions. For this reason data on the temperature and precipitation in New York City were obtained from the Weather Bureau, with the expectation of finding high precipitation in the months of the year when the cases were most numerous.

The general impression seems to be that most cases of rheumatism occur during damp cold weather, and this belief appears to be largely

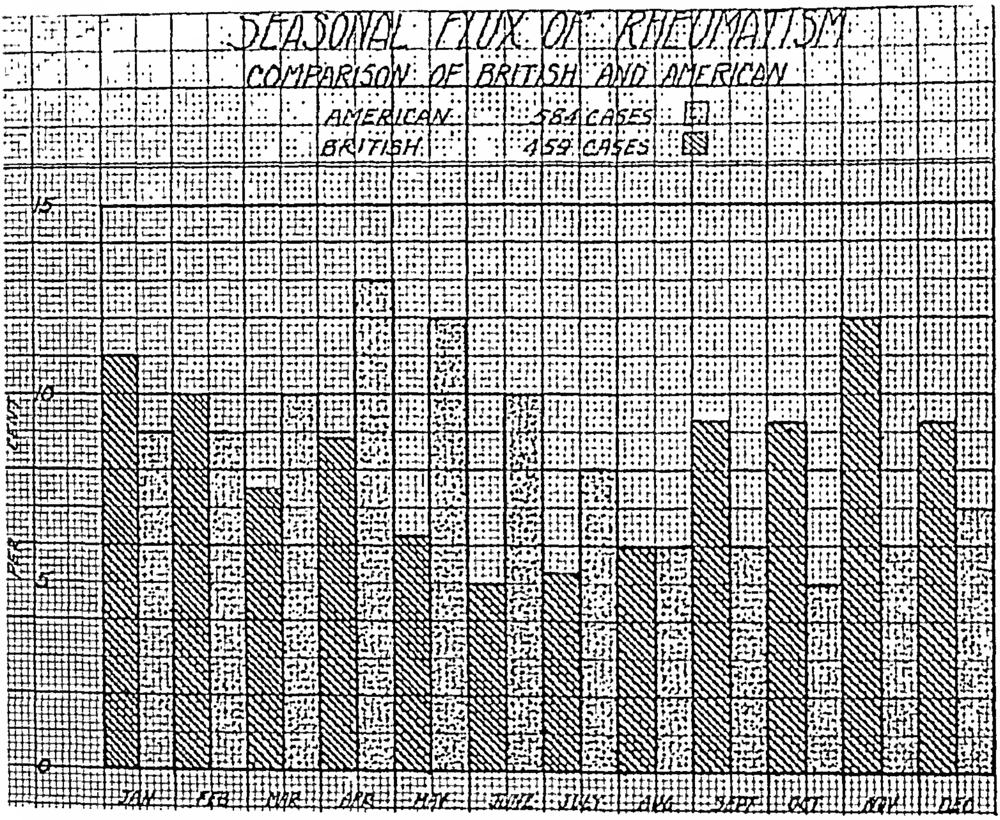

Fig. 3.—Taken from "Social Conditions and Acute Rheumatism" with American findings inserted for comparison.

based on the work of Young[2, 3] in England. He studied the annual rainfall and temperature in 55 counties in England and Wales in relation to the standardized death rate from rheumatic fever among individuals fifteen years of age and up. He states that "there is a distinct tendency for excess in rainfall to be associated with an increased death-rate from, and presumably an increased prevalence of, rheumatic fever. . . . the death-rate is higher and presumably the malady is more prevalent with an excess of cold weather during the year." Varying opinions had been stated before Young's study was made. Newsholme (quoted by Young) had come to the conclusion that heavy annual rainfall is associated with a low amount of rheu-

matic fever and small rainfall with an excessive amount, though he found no exact proportion. He also found that, on the whole, high temperature favored an increased amount of rheumatism. Gabbett (quoted by Young) concluded that it was difficult to make any connection between the state of the weather and the prevalence of disease in individual years but that the cases were numerous at the time of year when there was heavy rainfall and low temperature, i.e., at the end of autumn. Greenwood and Thompson (quoted by Young) concluded that rheumatism is associated with dry weather.

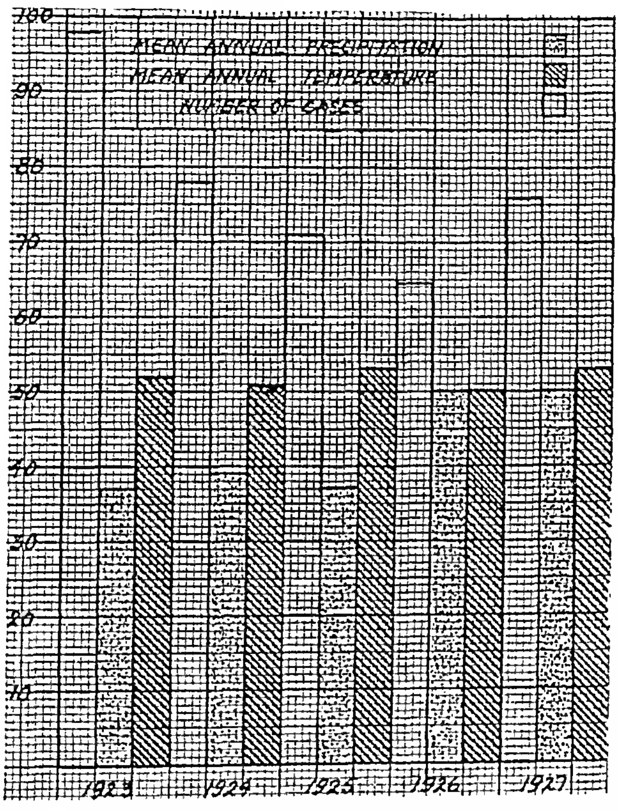

Fig. 4.—Comparison of mean annual temperature and precipitation 1923 to 1927 and number of cases admitted to wards during these years.

The figures used in this study are for precipitation, which includes both rain- and snow-fall.

Fig. 4 compares the mean annual temperature and the mean annual precipitation for the years 1923 to 1927, with the number of ward cases on the children's service at Bellevue Hospital for these years. The year which held the greatest number of cases had the lowest precipitation; the year with the fewest cases had the highest precipitation. There is little variation in the mean temperature, but the year with the highest mean temperature brought next to the lowest number of cases to the hospital.

Fig. 5 gives the monthly curve for the children admitted to Bellevue during the years 1923 to 1927, compared to the monthly mean precipi-

tation and temperature averaged for these years. Before combining the five years and getting the average, curves were made for each individual year, with results not essentially different from the averaged results. These curves appear to show that the greatest number of cases occur in the months when the precipitation is lowest and the temperature rising. This is exactly the opposite of what had been anticipated.

No conclusion can properly be drawn from this or any similar study as to the effect of meteorological conditions on the incidence of rheumatism. When accurate morbidity statistics are obtainable, it is pos-

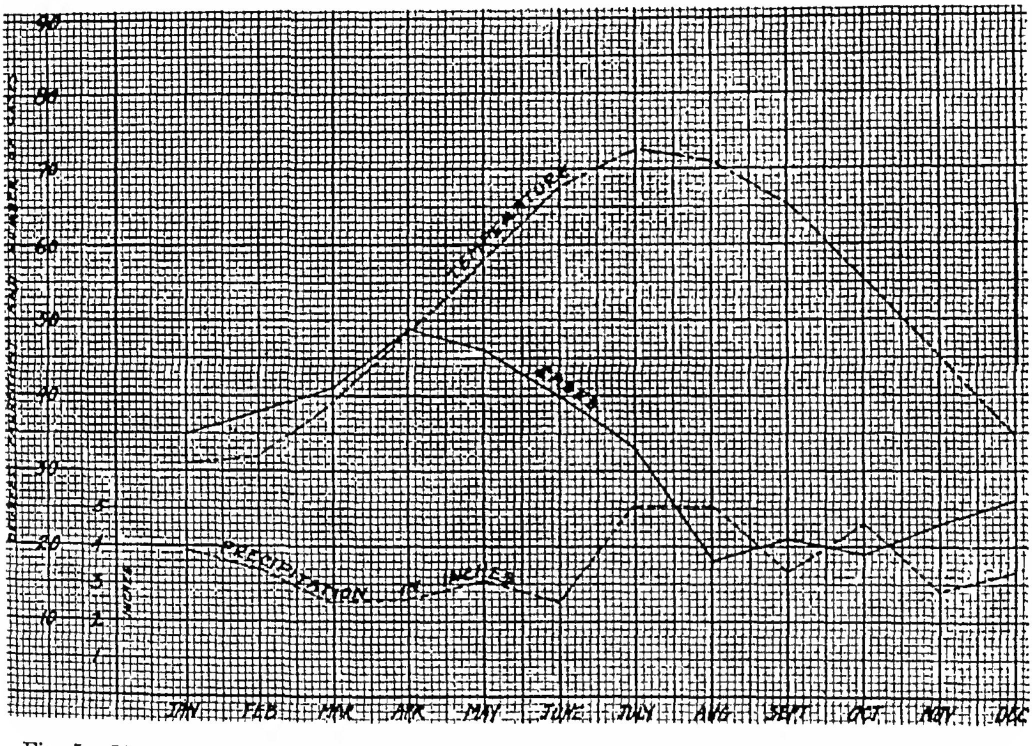

Fig. 5.—Monthly mean temperature and precipitation averaged for years 1923 to 1927, and number of cases admitted to wards during the months of these years.

sible that some correlation will appear, but for the present it can only be said that there appears to be little if any relation between the seasonal incidence of rheumatism, and precipitation, and temperature.

SUMMARY

Analysis by race of 506 children in the cardiac clinic at Bellevue Hospital and 511 children in the general pediatric clinic indicates that certain races in New York City, namely, Italian, Irish and native-born Americans, are somewhat more susceptible to rheumatism than certain other races. Certain other races, namely, Spanish, Armenian, and Jews, seem to be less susceptible.

Females are slightly more frequently affected with rheumatic heart disease than males.

The age at which most cases of rheumatism begin, without considering sex, is nine years. The average age at onset for boys is seven years, for girls nine years.

Twenty-one per cent of girls with rheumatic heart disease gave no history of rheumatic infection before the discovery of heart disease, while only 14 per cent of the boys gave no such history.

There is a definite seasonal incidence of rheumatism in New York City, which shows little variation in individual years. In general, the spring months show the highest incidence. For the five-year period studied, April and May contained the greatest number of cases. No correlation could be made between meteorological conditions and monthly incidence of rheumatism. In general, the height of the rheumatic season occurred at the time of year when the precipitation was lowest and the temperature rising, a finding contrary to that to be expected if Young's conclusions have general applicability.

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THE CLINICAL SIGNIFICANCE OF ABERRANT VENTRICULAR RESPONSE TO AURICULAR PREMATURE BEATS AND TO PAROXYSMAL AURICULAR TACHYCARDIA*

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INTRODUCTION

ONE of the most serious electrocardiographic findings in the study of heart disease is that of intraventricular block, either slight in degree or full bundle-branch block, a finding which represents important damage in the coronary circulation or in the myocardium. The fact that in experimental studies, aberrant ventricular responses (that is, intraventricular block) to auricular premature beats are obtained more readily when slight conduction changes are present due to asphyxia,[1, 4] and our own observation of this phenomenon in some patients with serious heart disease, suggested the possbility that aberrant ventricular responses to auricular premature beats may represent serious trouble with the conducting system or with the muscle of the heart. To throw further light on this point, the electrocardiograms of three hundred and eighty-seven consecutive cases showing auricular premature beats were carefullly reviewed. The patients concerned were in the wards or out-patient department of the Massachusetts General Hospital or were referred as private patients for special study. The electrocardiograms were taken over a period of thirteen and one-half years (1914 to 1928). One hundred and seven of these three hundred and eighty-seven cases showed aberrant ventricular responses of varying degrees. The electrocardiograms and the cases from which these records were obtained have been analyzed and the cases followed so far as possible.

In a clinical study of the ventricular response to auricular premature beats in a few cases from this laboratory some years ago White and Stevens[2] concluded that the degree of aberration in the ventricular response depends largely upon the degree of prematurity. Lewis[3] in 1909-10 first observed aberrant ventricular responses to auricular premature beats, without attempting to give an explanation. This same author[4] again in 1911-12 reported additional cases and first suggested the name "aberrant ventricular response," proposing the explanation that the appearance was caused by block in the ventricular portion of the conducting system. His first case by

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this time had been observed for two years. The degree of prematurity was considered important in relation to the degree of aberration. This is commented upon by Rosenthal[5] who reported a case at the same time. In 1924 in a paper on incomplete bundle-branch block, Stenström[6] reviewed the literature on aberrant ventricular response to auricular premature beats and concluded from experimental studies and clinical observations that this phenomenon may be aptly compared to the different stages in partial A-V block. He did not study the clinical significance of this finding. Lewis[7] has fully summarized experimental and clinical observations on this point up to 1925. The recent literature on premature beats has been chiefly concerned with the theories about their origin or with treatment. E. C. White[8] has studied one hundred cases of all varieties of premature beats, 45 per cent being associated with definite heart disease, and 55 per cent with no heart disease. D'Irsay[9] reviewed one hundred cases seen in hospital practice and made especial distinction between unifocal and multifocal origin of extrasystoles, presuming the former to be neurogenic and the latter due to an organic myocardial degeneration. The "multifocal" extrasystoles in that author's series showed a higher mortality and were associated with "some myocardial lesion, detected either by electrocardiograph or by autopsy." Wenkebach,[10] in his textbook, states that aberration of the ventricular complex following auricular premature beats is due to a variable recovery period and is without especial significance.

RESULTS OF PRESENT STUDY

Selecting from the total series of our three hundred and eighty-seven cases showing auricular premature beats those one hundred and seven cases with aberrant ventricular responses, we have divided them into four classes according to the degree of aberration shown. Several electrocardiograms showing auricular premature beats were sometimes obtained from a single case. Such a case has been grouped according to the greatest degree of abnormality of ventricular response shown to auricular premature beats. Altogether there were four hundred and forty electrocardiograms taken of the one hundred and seven cases showing abnormal ventricular responses to auricular premature beats. In Class I two cases showed normal as well as slightly aberrant T-waves following auricular premature beats, while Classes II, III and IV included twelve, sixteen and three cases respectively which showed at the same time lesser degrees of aberrant response than that for which they were placed in the given class. Class I (Fig. 1) includes only those cases (16) with but a slight change in the T-wave following an auricular premature beat, Class II (Fig. 2) those cases (55) showing slight changes either in the QRS complexes alone or in both QRS and T. Slight changes in the T-wave consist of

depression of the wave as compared to other T-waves following normal auricular waves in the same tracing. Slight QRS changes consist of heightening or shortening of R, or of deepening or shortening of S as compared with those QRS complexes which follow normally placed P-waves. Class III (Fig. 3) (30 cases) consists of moderate (more than slight) changes in QRS and T-waves following auricular premature beats. Finally, Class IV (Fig. 4) is made up of six cases exhibiting very marked changes in amplitude with widening of the QRS interval and usually with profound changes in the T-wave. Forty cases have

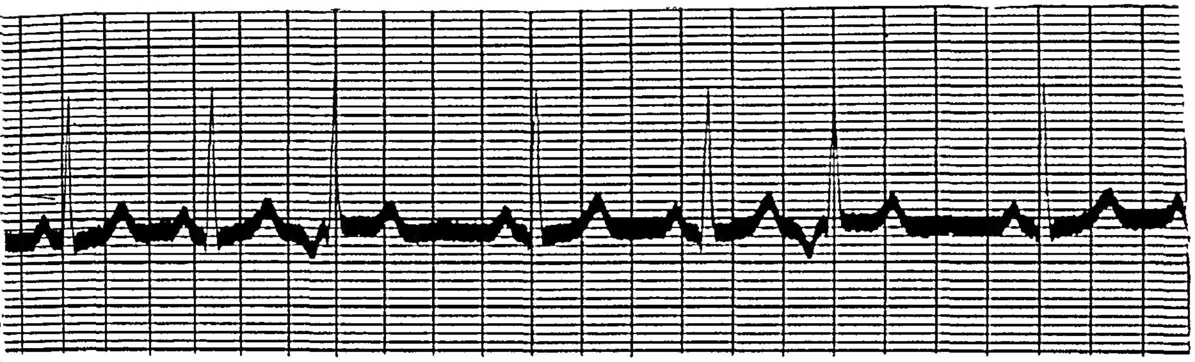

Fig. 1.—The third and sixth ventricular complexes illustrate the type of ventricular response to auricular premature beats included in Class I (referred to in the text); slight changes in T-wave and S-T interval only. Lead II. (In this as in the other illustrations time intervals equal fifths of a second. Amplitude is expressed by divisions marking off intervals of 10-¹ volt.)

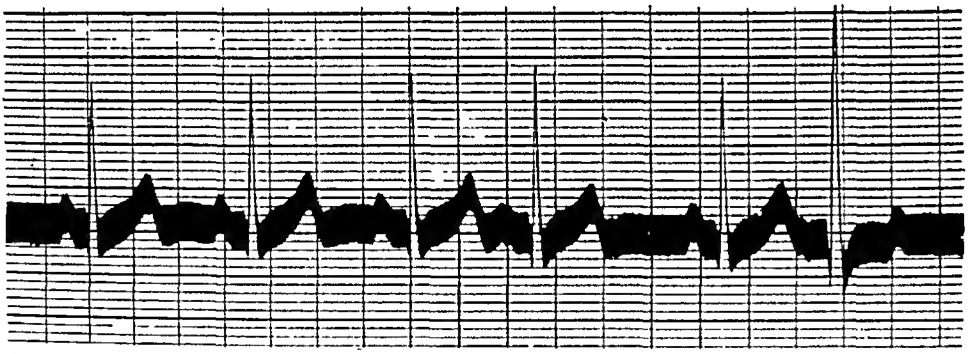

Fig. 2.—The fourth ventricular complex represents those premature beats used as controls while the sixth complex represents Class II, slight changes in both QRS and T-waves. Lead II.

been studied as "normal controls" (Fig. 2)—that is, normal so far as the ventricular response to auricular premature beats is concerned.

The age and sex distribution for this series is given in Table 1. Both in the series of cases with varying degrees of aberrant responses and in the control group showing normal responses, the occurrence is greater among males (56 to 36 in the former, 27 to 11 in the latter). The age distribution for all four classes as well as for the normal controls is approximately the same, in all cases the incidence of the auricular premature beats being greatest between the ages of fifty and seventy years.

The relation of degree of prematurity to degree of aberration is demonstrated very clearly in Table II. The figures give the average of the percentage relation of time intervals of P-P′ to P-P; those premature beats represented by the smaller figures have fallen earlier in diastole.

It is interesting to note here the occurrence of intraventricular block during the course of *paroxysms of auricular tachycardia.*

Transient disturbances of this nature of less importance have been noted; as for example in the case of a nurse who developed for a few

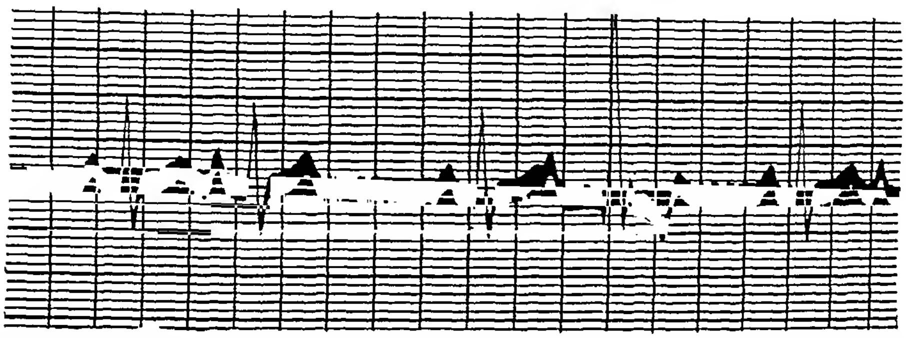

Fig. 3.—The fourth ventricular complex falls in Class III, moderate QRS and T-wave changes. The second ventricular complex shows essentially normal QRS and T-waves. Lead II.

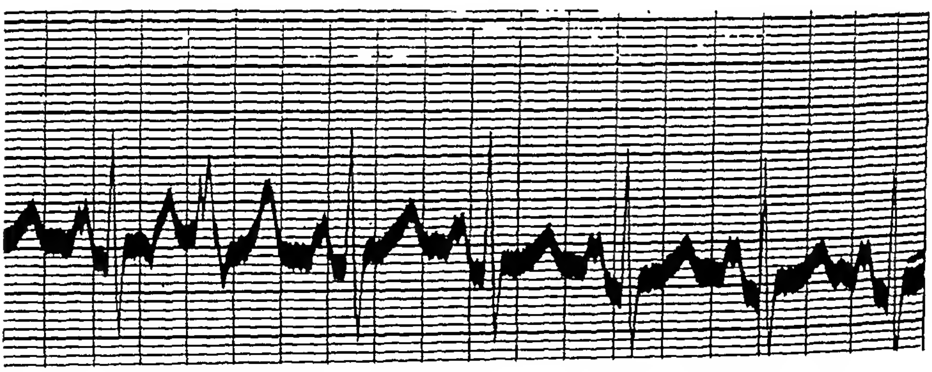

Fig. 4.—The second ventricular complex shows marked aberration, Class IV. Lead II.

minutes left bundle-branch block at the height of a paroxysm of auricular tachycardia of extreme degree (both auricular and ventricular rates were 273), reported by White and Stevens.[2] Now, thirteen years later, this nurse is working and in good health except for rare intervals of disturbed heart rhythm lasting a few hours at a time (ectopic auricular tachycardia, generally with auriculoventricular block). Three other cases, four in all, of aberration in the ventricular complexes in the course of a paroxysm of auricular tachycardia have been observed in a series of 73 cases of paroxysmal auricular tachycardia. One of these patients, a man aged sixty-four years (diagnosis rheumatic heart disease, irritable heart, aortic re-

gurgitation, Stokes-Adams syndrome, partial A-V block, S-A block, paroxysmal tachycardia, auricular and ventricular premature beats), has had heart trouble since rheumatic fever forty-three years ago. Stokes-Adams symptoms have been present about eight years. Our

TABLE I

SEX AND AGE DISTRIBUTION*

			AGE								
CLASS	M.	F.	1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90
I	7	5		1			3	2	5	1	1
II	26	18	1	6	4	1	8	8	8	6	
III	19	11		1	4	2	4	6	3	1	
IV	4	2			1			1	1		
Total	56	36	1	8	9	3	15	17	17	8	1
Controls	27	11	0	5	3	2	2	6	9	3	
Grand Total	83	47	1	13	12	5	17	23	26	11	1

*Discrepancy between total numbers in the various tables is due to cases omitted because of incomplete data or of other difficulties.

TABLE II

DEGREE OF PREMATURITY

CLASS	I	II	III	IV	CONTROL
No. of cases	13	53	30	6	39
Relation of P-P′ to P-P interval per cent*	64.4	61.4	56.6	48.2	66.0

*P-P′ is interval between normal auricular complex and the premature auricular deflection; P-P is the normal time interval between beats.

TABLE III

RELATIONSHIP OF P′R′ TO PR INTERVALS

CLASS	I	II	III	IV	CONTROL
No of cases	16	48	27	6	40
P′R′ interval in P.B.					
Longer than normal PR	1	10	11	2	4
Shorter than normal PR	7	20	5	1	12
Equal to normal PR	8	18	11	3	24

TABLE IV

HEART RATE

CLASS	I	II	III	IV	CONTROL
No. of cases	16	55	30	6	40
Average rate	94.0	88.3	92.3	82.0	90

records show auricular paroxysms with intraventricular block during the paroxysm in October, 1925. In April, 1928, the patient's gall bladder was removed and he appears to be doing fairly well in respect to his heart, although he has developed permanent block and auricular fibrillation. A third case, a man aged thirty-one years (diagnosis auricular and ventricular premature beats, paroxysmal tachycardia),

showed slight aberration in the course of paroxysms of tachycardia in October, 1914, more definite aberration under the same conditions in 1924. In March, 1928, he was perfectly well except for occasional extrasystoles. The fourth patient, a man twenty-seven years old, first showed paroxysmal auricular tachycardia with aberrant responses in January, 1919. He was well and working as a meat cutter in November, 1927, having since, however, shown a paroxysm of ventricular origin.

In Table III we have tabulated the different classes according to the relation of P'R' to PR, whether longer, shorter, or equal. It

TABLE V

Q-T INTERVAL OF PREMATURE BEAT COMPARED TO THAT OF NORMAL BEATS IN THE SAME TRACING

CLASS	I	II	III	IV	CONTROL
No of cases	15	51	27	6	36
QT Shortening	9	26	14	2	16
QT Lengthening	1	7	6	2	0
QT Unchanged	5	18	7	2	20

TABLE VI

FOLLOW-UP DATA

CLASS	NUMBER FOLLOWED	LIVING	DEAD
I	12	8	4
II	21	9	12
III	6	3	3
IV	3	2	1
Control	21	11	10

appears, as might be expected, that the later in diastole the premature beat falls the less likely is the P-R interval of the premature beat to be prolonged. The fact that a considerable number of the P-R intervals in the case of the premature beats are shorter than the P-R intervals of the normal beats probably represents a position of the new ectopic auricular pacemaker nearer the A-V node than is the normal sino-auricular pacemaker.

The average rate of the heart in each class (Table IV) does not appear to be especially important in this connection. The significance of premature beats occurring with rapid heart rates will be the subject of a later communication from this laboratory.

In Table V we have given the data on changes of the Q-T interval (i.e., from the beginning of Q to the end of T) in premature beats. This interval represents the duration of ventricular systole. Shortening of the Q-T interval occurs more often with the aberrant responses. Shortening of systole is the common finding with increased heart rates normally and would be expected to be of frequent occurrence in the case of auricular premature beats, as we have found it to be.

Associated changes in the electrocardiogram, other than changes in the premature beat, were of no especial significance except that the series of records with aberrant auricular premature beats showed more T-wave abnormalities and a higher incidence of axis deviations than did the control series.

The number and variety of primary diagnoses represented in the series make it difficult to draw any conclusions, but we have found no significant difference in the gravity of the patient's condition as indicated by the diagnosis in the cases making up the different classes and control series. For instance, among the miscellaneous cases without heart disease are included lobar pneumonia, lupus vulgaris, acne vulgaris, tenia saginata, gall bladder disease, xeroderma, psychoneurosis, and duodenal ulcer. A definite diagnosis of heart disease was made 8 times in Class I (16 cases; 50 per cent); 19 times in Class II (55 cases; 34 per cent); 6 times in Class III (30 cases; 20 per cent); once in Class IV (6 cases; 16 per cent); and 16 times among 40 control cases (40 per cent).

Finally, in Table VI may be found the cases which have been followed, with the number living and the number dead. So far as we are able to judge, the end-results in those cases showing aberrant ventricular responses to auricular premature beats are not other than may be expected from associated findings or different from any group of cases showing auricular premature beats with normal responses.

SUMMARY AND CONCLUSIONS

1. A study has been made at the Massachusetts General Hospital of three hundred and eighty-seven consecutive cases with electrocardiograms showing auricular premature beats. Of this number the one hundred and seven cases showing aberrant ventricular responses to these auricular premature beats (with normal response to normal auricular stimuli*) have been analyzed. A study has also been made of the electrocardiograms of seventy-three cases of auricular paroxysmal tachycardia.

2. Aberration and the degree of aberration (intraventricular block) in the ventricular response to an auricular premature beat, have been found to depend upon the degree of prematurity and so far as we have been able to judge the finding of aberrant ventricular responses to auricular premature beats does not alter appreciably the prognosis in a given case.

3. Aberration in the ventricular complexes during the height of a paroxysm of auricular tachycardia appears not to be serious, judging from a review of four such cases found among a total of seventy-three patients with auricular paroxysmal tachycardia studied by us.

*Except for a few cases which showed constant intraventricular block with increased aberration following auricular premature beats.

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THE POSITIVE CENTRIFUGAL VENOUS PULSE*

A Clinicopathological Correlation

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In 1925 Kerr and Warren[1] reviewed the literature on the peripheral venous pulsations and added valuable evidence of their clinical importance in the diagnosis of tricuspid insufficiency. The following year occasion was taken to report a new expedient in demonstrating the positive centrifugal venous pulse in the peripheral veins, namely, elevation of the forearm to a distance above the heart equivalent to the venous pressure.[2] This procedure simply serves the purpose of overcoming hydrostatic pressure to the end that such waves as are initiated in the great venous trunks on right ventricular contraction in the presence of incompetency of the tricuspid valve, are better transmitted peripherally. Otherwise the force necessary to overcome the inertia of the column of returning blood may dissipate the feeble centrifugal venous waves. These observations strictly confirmed the studies of Kerr and Warren in attributing a virtual pathognomonic value to this sign in tricuspid insufficiency.

Three of the cases reported in that communication came to necropsy and the measurements of the circumference of the tricuspid orifices (12, 12, and 13.5 cm. respectively) suggested an objective proof of the accuracy of the above conclusion. Since that time 12 patients with congestive heart failure showing the positive centrifugal venous pulse during life have died. The data relative to the pertinent clinical and pathological findings are tabulated below:

The range of measurement of the circumference of the tricuspid orifice was from 11.5 to 16.5 cm. with an average of 13.5 cm. Vierordt[3] gives 12 cm. as the normal figure for the circumference of the tricuspid orifice in the female and 12.2 (Wulff) to 12.7 cm. in the male. While these figures are deemed too high by certain pathologists, still they may serve in the present relation. Clearly 2 of 3 female subjects showed tricuspid measurements above the standard for their sex, while 8 of 9 males exceeded the above stated normal. In any event the majority of cases in this small series, showing a positive centrifugal venous pulse, had actual widening (relative insufficiency) of the tricuspid orifice at necropsy, and it is not necessary in such cases to invoke the second explanation of relative insufficiency, namely, the traction of the chordae

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TABLE I

DATA ON CASES OF DECOMPENSATION

NO.	AGE	SEX	CLINICAL DIAGNOSIS	POSITIVE CENTRIFUGAL VENOUS PULSE	CIRCUMFERENCE OF TRICUSPID ORIFICE (CM.)	HISTOLOGY—MYOCARDIUM
1	52	M	Myocardial degeneration; auricular fibrillation; relative tricuspid and mitral insufficiency.	+	14.6	Perivascular and interstitial fibrosis; hypertrophy.
2	75	M	Arteriosclerosis; myocardial degeneration; cardiac hypertrophy and dilatation; auricular fibrillation; relative mitral and tricuspid insufficiency.	+	13.0	Sclerosis of vessels; fibrosis; hypertrophy.
3	16	F	Rheumatic endocarditis (aortic and mitral) and pericarditis; myocardial degeneration.	+	12.5	Hypertrophy; fibrosis; necrosis; Aschoff bodies.
4	44	M	Chronic endocarditis (aortic and mitral); acute pericarditis; cardiac hypertrophy; myocardial degeneration; relative tricuspid insufficiency.	+	15.5	Hypertrophy; fragmentation; scars.
5	40	M	Tertiary syphilis; aortitis with aneurysm; aortic insufficiency; cardiac hypertrophy and dilatation; relative tricuspid insufficiency.	+	14.0	Anemic infarction with scarring; interstitial fibrosis.
6	32	F	Adhesive pericarditis; myocardial degeneration; relative tricuspid insufficiency.	+	11.5	Hyalin necrosis; atrophy
7	86	M	Arteriosclerosis; myocardial degeneration; auricular fibrillation.	+	11.5	Fibrosis; hypertrophy; perivascular lymphoid infiltration.
8	78	M	Arteriosclerosis; hypertension; myocardial degeneration; auricular fibrillation; cardiac hypertrophy.	+	13.0	Anemic infarcts; hypertrophy; scars.
9	62	M	Arteriosclerosis; hypertension; cardiac hypertrophy; myocardial degeneration; auricular fibrillation; relative tricuspid insufficiency.	+	13.5	
10	74	M	Arteriosclerosis; hypertension; cardiac hypertrophy; myocardial degeneration; relative mitral and tricuspid insufficiency.	+	14.0	Hypertrophy; necrosis; nuclei vacuolated, or absent in places.
11	68	F	Chronic endocarditis (mitral); cardiac hypertrophy and dilatation; myocardial degeneration; relative tricuspid insufficiency.	+	12.5	Fibrosis; hypertrophy; edema.
12	63	M	Toxic adenoma of thyroid; myocardial degeneration; cardiac hypertrophy and dilatation; auricular fibrillation; relative mitral and tricuspid insufficiency.	+	16.5	Hypertrophy; fibrosis; lipochromatosis.

tendineae on the valve margin through right ventricular stretch. The converse is not true. Absence of a positive centrifugal venous pulse does not rule out tricuspid insufficiency, since in a control group of 12 cases of congestive heart failure without this sign coming to necropsy in the same period of time, 8 showed tricuspid measurements exceeding the standard figures for their respective sexes. This failure to demonstrate the positive centrifugal venous pulse in the presence of anatomical insufficiency of the tricuspid valve may be explained by local edema in the arms, technical difficulties in observing minor venous waves, unusual integrity of the valves of the veins, right ventricular contractions too feeble to propagate waves into the peripheral veins or absence of residual blood in the right auricle.

A word of explanation is necessary with regard to the last mentioned point. Mackenzie on repeated occasions[4, 5, 6] remarked the necessity for a residuum of blood in the right auricle through which the regurgitant blood from the right ventricle might act, before venous pulse waves could be anticipated in the peripheral bed. "That [the ventricular form of venous pulse] is a sign of tricuspid regurgitation there is no doubt, but it is a sign of far greater significance, namely that the auricle does not precede the ventricle in the cardiac cycle."[6] Obviously from a mechanical or hemodynamic standpoint no circumstance would favor this situation more effectively than auricular fibrillation. Only 6 of the reported group of 12 cases of decompensation with a positive centrifugal venous pulse, coming to necropsy, had shown auricular fibrillation. Hence the phenomenon may occur in the absence of auricular fibrillation, provided the other factors for the production and propagation of the retrograde venous wave be present.

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STATISTICAL STUDIES BEARING ON PROBLEMS IN THE CLASSIFICATION OF HEART DISEASE

III. Heart Disease in Children*

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INTRODUCTION

THE wider interest in heart disease as a public health problem has in the past few years stimulated a renewed and intense interest in the etiology, pathology, and natural history of heart disease in children, particularly in that of the rheumatic variety. Cohn[1] in a recent issue of this journal has reviewed in detail published data bearing on the subject. He indicates the inadequacy of the information at present available and suggests the collection of data in a uniform manner so that necessary and more accurate information on the important phases of the problem may be obtained.

In this investigation an attempt was made to collate some basic data concerning the natural history of heart disease in children. The study is based on the statistical analysis of the case histories‡ of five hundred children observed in a clinic under the same medical supervision during a period of ten years. It presents data of interest on some of the problems of heart disease during the period ranging from childhood to adolescence. Of particular importance is the information obtained on the natural history of rheumatic infection in its relation to heart disease.

A consideration of data collected from clinical history records must always take into account obvious factors of error. In this investigation every effort was made to reduce these to a minimum. The medical supervision was uniform and the records were taken on special charts by trained workers. A number of children were observed from birth in the general clinic and about 150 were observed daily in special classes in school for a period of years.

Period of Observation.—The investigation covers a period of ten years (1916-1927). An attempt was made to obtain a final record of every patient living in 1927 (Table I). This was possible in all but

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†Working on behalf of the Committee on Research of the Heart Committee, New York Tuberculosis and Health Association.

‡The clinical charts recommended by the New York Heart Committee described in a recent issue of this journal have been used since 1923. All the old records were transcribed to these forms. The use of these charts has made this statistical analysis possible.

17 per cent of the patients, who were not located. During the period of observation 10.8 per cent of the patients died. In 72.2 per cent a final record was obtained, so that in 83 per cent a complete record of the course of the disease to death or to 1927 was secured. Sixty-one and six-tenths per cent of the children were under continuous observation for a period less than three years and 38.3 per cent over a period ranging from three to ten years.

Age Distribution.—The ages ranged from infancy to twenty-two years. On admission, 12 per cent of the children were under six years of age and 50 per cent were from six to ten years of age. On final observation, 38 per cent were from eleven to fourteen years and 25 per cent from fifteen to twenty-two years of age (Fig. 1).

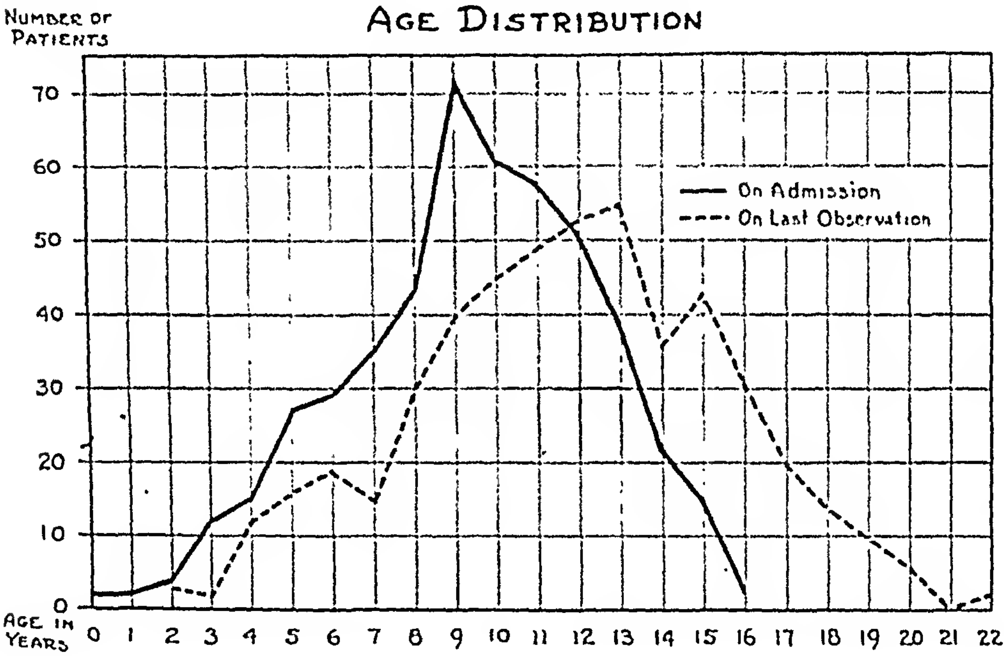

FIG. 1.

Etiology and Sex Distribution.—On first observation twenty-five children were classified as harboring possible heart disease (that is to say, there were negative histories, slight heart enlargement and persistent systolic murmur in the second to fourth left interspace—Class E). Of these children, twenty retained the same physical signs over the period of observation (Table II). This group is small in this series but it is representative of a large group which was under observation but is not included in this report. These children are also representative of cases with so-called inorganic or functional murmurs which are found in the course of school examination and form about one-half percent of the reported cases of heart disease in school children.[2] It is suggested that these childern may have some minor congenital malformation responsible for the persistent physical signs.

TABLE I

ETIOLOGY AND DISPOSITION OF CASE

ETIOLOGY (FINAL OBSERVATION)	% OF TOTAL CASES	TOTAL		UNDER CONTINUOUS OBSERVATION		DIED		INACTIVE					
								RETURNED FOR EXAMINATION		REPORTED ON		NOT LOCATED	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Rheumatic	79.0	395	100	187	47.3	47	11.9	47	11.9	57	14.4	57	14.4
Unknown	5.4	27	100	6	22.2	2	7.4	4	14.8	8	29.7	7	25.9
Class E	4.2	21	100	4	19.0	1	4.8	3	14.3	7	33.3	6	28.6
Congenital and Rheumatic	3.6	18	100	8	44.4	3	16.7	1	5.6	2	11.1	4	22.2
Congenital	7.6	38	100	16	42.1	1	2.6	5	13.2	5	13.2	11	28.9
Bacterial	0.2	1	100										
Total	100.0	500	100	221	44.2	54	10.8	60	12.0	80	16.0	85	17.0

Twenty-seven patients presented definite organic heart disease of unknown etiology (Table I). It is possible that they may have been rheumatic, but there was no evidence of any manifestation of rheumatic infection during the period of observation. It is suggested that heart disease in these children may be the result of some unknown or unrecognizable infection in infancy.[3]

Fifty-six, or 11.2 per cent, of the children were cases with congenital heart defect. Eighteen, or 3.6 per cent, of these also gave a complicating rheumatic history (Table I). Five had brothers and sisters with congenital heart defects. This incidence of 11.2 per cent may be considered as representative of the usual ratio of cases of congenital heart disease to the total number of cases of heart disease in children over the age of two years. Infants under two years with congenital heart defects were not included in this report.* The diagnosis of the particular congenital malformation is difficult to make and unreliable, since various cardiac malformations have been found at autopsy in cases that presented identical physical signs.† In 5 children the defect was recognized in the first year of life; in 12, between the second and the fifth year, and in the remaining 39 between the sixth and the thirteenth year. Forty-four children were well developed and in good general health. Four exhibited marked cyanosis, and in 8 general physical development was delayed. There were 4 deaths in this group, one from bronchopneumonia at the age of three years, and 3 from rheumatic heart disease at the ages of eight, sixteen, and seventeen years respectively.

There was one patient with organic heart disease of known bacterial etiology. This patient was observed before and after infection with diphtheria; the attack was complicated by post-diphtheritic paralysis.

*The London School[4] report gives the incidence of congenital heart disease as 11 per cent of the total cases of organic heart disease and the Bristol School[5] reports an incidence of 11 per cent of a total of 202 cases of organic heart disease.

†Schloss, O. M. and Wilson, James: Congenital Heart Disease: Clinical and Pathological Studies, Am. Jour. Dis. Child, (to be published).

The heart remained definitely enlarged without clinical evidence of valvular disease. The patient was observed for eight years and at no time during that period showed any manifestation of rheumatic infection.

The remaining cases (395 or 79 per cent) presented a rheumatic history (Table 1). Of these, three-quarters suffered from organic heart disease. This is in marked contrast to the incidence of heart involvement (29.8 per cent) noted in a series of 473 children observed

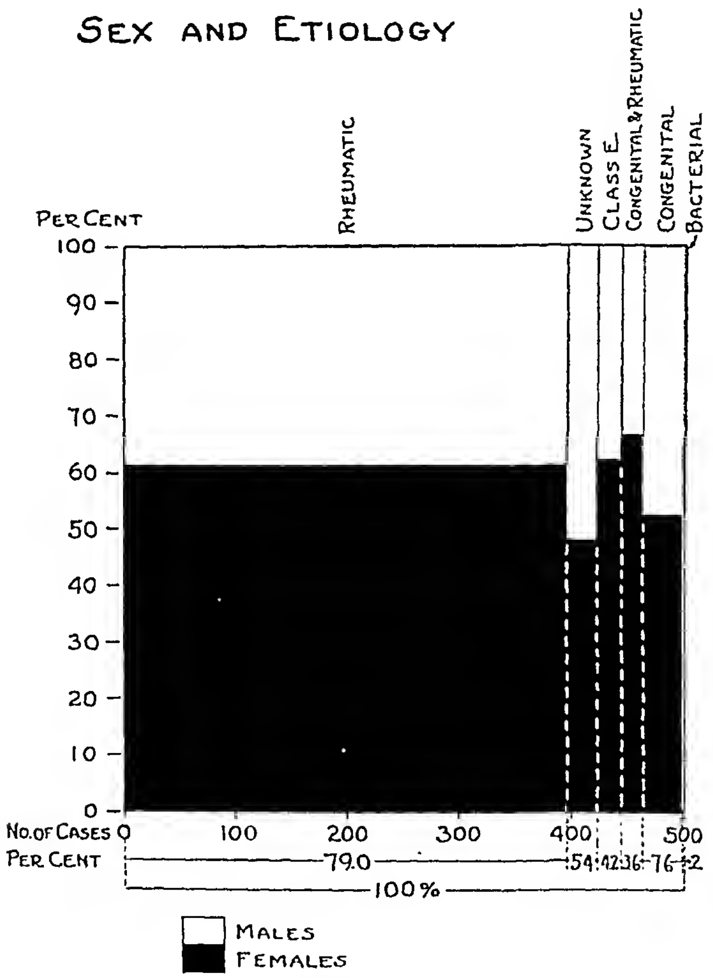

Fig. 2.

over a period of from two to six years at St. Thomas' Hospital.[9] The remaining were "potential" heart cases. This incidence confirms the general opinion that rheumatic infection is the most common etiological factor in heart disease in children. Recently, Wyckoff and Lingg[6] found from a statistical study of 1000 cases of organic heart disease that "in the second decade 80 per cent of the cases were of rheumatic etiology."

Correlation between sex and etiology shows for the total of 500 children a predominance of females (60 per cent females and 40 per

cent males). There was an almost equal sex distribution among children with heart disease of unknown etiology and congenital heart disease, whereas there was a predominance of females among those with rheumatic heart disease—61.2 per cent females as against 38.8

TABLE II.

RELATIVE DIAGNOSIS ON FIRST AND LAST OBSERVATION

FIRST OBSERVATION		LAST OBSERVATION DIAGNOSIS									
				CONGENITAL MALFORMATION							
DIAGNOSIS	% OF TOTAL	TOTAL		CONG. MALF. ONLY		CONG. MALF. & RHEUM. HIST.		CONG. MALF. & VALV. DISEASE		TOTAL	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Congenital Malformation only	8.4	42	100	36	85.8	4	9.5	2	4.7	42	100
Congenital Malformation and Rheum. History	1.6	8	100			6	75.0	2	25.0	8	100
Congenital Malformation and Valvular Disease	.8	4	100					4	100	4	100
TOTAL	10.8	54	100	36	66.8	10	18.5	8	14.7	54	100
Mitral Insufficiency	31.5	157	100								
Mitral Insufficiency / Mitral Stenosis	17.0	85	100								
Mitral Insufficiency / Aortic Insufficiency	1.0	5	100								
Mitral Insufficiency and Stenosis / Aortic Insufficiency	2.4	12	100								
TOTAL	51.9	259	100								
Acute Rheum. Carditis	.6	3	100								
Possible Heart Disease (Class E)	5.0	25	100	2	8.0					2	8.0
Negative Heart	14.4	72	100								
Systolic Murmur	2.2	11	100								
Enlargement of Heart	11.9	60	100								
Systolic Murmur and Enlargement	3.2	16	100								
TOTAL	31.7	159	100								
TOTAL	.	500	100	38	7.6	10	2 0	8	1.6	56	11 2

per cent males (Fig. 2). This is in accord with the experience of other observers. The reason for it is at the present time unknown.

THE NATURAL HISTORY OF RHEUMATIC INFECTION IN ITS RELATION TO RHEUMATIC HEART DISEASE

*Social History.**—A consideration of social, environmental, and economic conditions in 329 cases of rheumatic etiology has suggested a study of certain matters which we wish to discuss in detail.

1. *Economic Status.*—The majority of the children came from moderately well-to-do homes of the industrial laboring class of the city. In 65 per cent of the cases the family budget was estimated as ade-

*Report from the Social Service Department of the New York Nursery and Child's Hospital.

quate to conditions for decent living ($1500.00 to $2600.00 per year). In 72 per cent the homes were clean. In 50 per cent they were neither overcrowded nor damp. It may be important to note that the location of about half of the homes was within three blocks (400 yards) of the Hudson river. Evidence of dampness was found in only 23 per cent of them. These data are in accord with those reported by the Medical

TABLE II—CONTINUED

RELATIVE DIAGNOSIS ON FIRST AND LAST OBSERVATION—CONTINUED

LAST OBSERVATION DIAGNOSIS																							
VALVULAR DISEASE										ACUTE RHEUM. CARDITIS		POSSIBLE HEART DISEASE (CLASS E)		POTENTIAL									
M. I.		M. S. M. I.		M. I. M. S. A. I.		M. I. A. I.		TOTAL						NEG. HEART		SYSTOLIC MURMUR		EN-LARGE-MENT		SYS. MUR & ENL.		TOTAL	
NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
101	64.4	48	30.6	1	.6	2	1.2	152	96 8			1	0 6	2	1.3			2	1 3			4	2.6
		71	83 5			13	15.3	84	98 8									1	1.2			1	1.2
				4	80 0	1	20 0	5	100														
						12	100	12	100														
101	39.0	119	46.0	5	1.0	28	10 8	253	97.7			1	0.4	2	.8			3	1.1			5	1.9
1	33.3			1	33 3			2	66.6	1	33.3												
3	12.0							3	12.0			20	80.0										
21	29.2	5	6.9					26	36.1	2	2.7			24	33.3	1	1.4	13	18.1	6	8.3	44	61.1
5	45.4	1	9.1					6	54.5					1	9.1	4	36 4					5	45.5
21	35.0					1	1.6	22	36.6									29	48.3	9	15 0	38	63.3
4	25.0	1	6.2					5	31.2							1	6 2	1	6 2	9	56 3	11	68.7
51	32.1	7	4.4			1	0.6	59	37.1	2	1.3			25	15.7	6	3.8	43	27.0	24	15.1	98	61 6
156	31.2	126	25.2	6	1 2	29	5 8	317	63 4	3	0 6	21	4.2	27	5 4	6	1 2	46	9 2	24	4 8	103	20 6

Research Council in *Social Conditions and Acute Rheumatism,* in which "the greatest incidence of rheumatism was found in the better class of industrial homes." The report of the Housing Inquiry showed "a slightly more frequent dampness in the houses of rheumatic families and suggested proximity to waters and river courses as a possible factor. Overcrowding or extreme poverty were not prime factors, except as the resistance is lowered by unfavorable conditions of living."[7]

2. *Race.*—Thirty-two per cent were of Irish stock; 19.5 per cent were American born; 12.5 per cent were Italian, and 4.1 per cent were Jewish. Only 18, or 4.6 per cent, of the children were colored, although

the clinic draws from a colored district.* The remainder were distributed among Germans, 8.8 per cent; Russians or Poles, 4.4 per cent, and others, totalling 13.5 per cent. The large proportion of Irish children should not be construed as necessarily indicating that this racial group is particularly susceptible to rheumatic infection, but rather as due to the fact that our clinic is situated in a section of the city that has a large Irish population.

3. *Physical Characteristics.*—A review of certain physical characteristics showed that 22.0 per cent of the children were of the brunette type, that is to say, had dark eyes and dark hair; 16.7 per cent of the blonde type, with blue eyes and light hair; 50.0 per cent of a mixed type, and but 2.9 per cent had red hair and blue eyes. The studies reported by St. Thomas' Hospital indicated that darker types tend to show a greater predisposition to rheumatism than the fairer types. This is at variance with the conclusion of Shrubsall that, at St. Bartholomew's Hospital, rheumatic affections show a special predilection for the pure blonde type.[7] This divergence in various reported series is probably related to the racial constitution of the groups studied. In our series the large number of children of mixed type seems to be accounted for by the large number of Irish and American children in our group.

4. *Heredity.*—Thirty-six per cent of the children had rheumatic brothers or sisters. In the St. Thomas' Hospital report,[9] a family incidence of rheumatism was obtained in 36.1 per cent and in Coombs' analysis,[10] an incidence of 50 per cent. St. Lawrence[11] found a family incidence of heart disease and acute rheumatic fever in 29 per cent and 24 per cent respectively; Faulkner and White[12] reported a family incidence of rheumatic affections in 8.8 per cent. The question of possible contagion in the families of the children in our series has been considered, but no direct evidence of such a factor was noted during the period of observation. The result of the British inquiry as to the element of contagion states our present view: "On the whole it cannot be said that there is in the facts collected any conclusive evidence of contagion though many of the facts are consistent with this view."

MANIFESTATIONS OF RHEUMATIC INFECTION†

An analysis was made of the records of 413‡ children who presented a rheumatic history. In their histories the following manifestations were regarded as evidence of the existence of rheumatic infection: polyarthritis, growing and joint pains, chorea, acute carditis, and sub-

*Wood, Jones, and Kimbrough[8] found that rheumatic heart disease "seemed to be less common among the colored people than the white people of Virginia." Unfortunately we could find no other direct observations recorded on this subject.

†The term Rheumatic Infection is used although it is appreciated that the evidence of its infectious nature is at present not conclusive.

‡This includes the 18 cases of congenital heart disease complicated by rheumatic infection.

cutaneous nodules. Tonsillitis was not included here as a manifestation of rheumatic infection because of the difficulty in differentiating, from a history between severe pharyngitis occurring with upper respiratory infections in young children, and frank tonsillitis assumed to be of a rheumatic nature. The occurrence of other manifestations, such as urticaria, purpura, and epistaxis, have likewise not been included.*

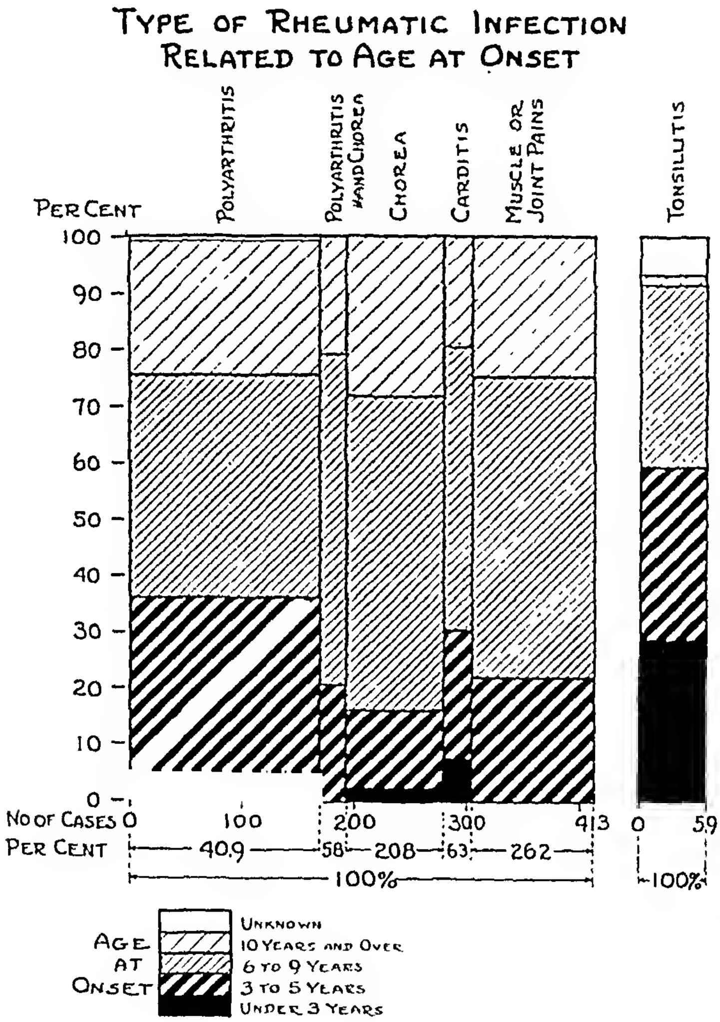

Fig. 3.

1. *Age at Onset.*—Before taking up the various manifestations of rheumatic infection we shall consider the clinical course of the disease, as a whole. It was found that, regardless of the particular kind of manifestation, the initial manifestation of infection occurred in the age group comprising the years six to nine, in about one-half of the cases (Fig. 3). In Mackie's[13] series the incidence curve of initial infection differs from this one in that it rises to a peak of 23.9 per cent in the group between the ages of six and nine years, 23.1 per

*In a previous publication an analysis of 185 case records shows various erythemas or skin lesions in 8 per cent and recurrent epistaxis in 11 per cent.

cent between ten and fifteen years and then slowly but progressively falls. It must be remembered, however, that Mackie's figures are not directly comparable with ours, in so far as our group is confined to children, whereas his includes adults. Histories obtained from adults are apt not to include the early complaints of childhood, which may account for the later dates of onset in Mackie's series. Ninety-eight and four-tenths per cent of our cases had their initial infection before they reached the age of fifteen, and almost 50 per cent of Mackie's cases had their first attack of rheumatic infection after the age of fifteen years was reached.

Fig. 4 shows the distribution of these 413 cases according to the age at which the first infection appeared. It may be seen that, begin-

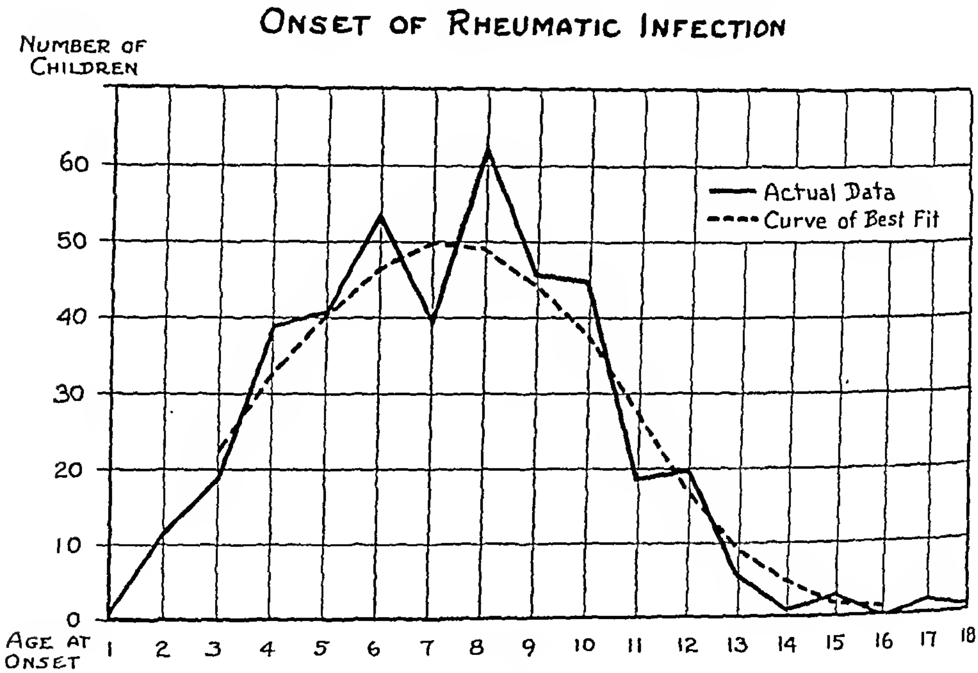

Fig. 4.

ning with the preschool ages, the curve gradually rises to the age of about six, remains high, up to the age of nine and declines thereafter. The average age at onset was found to be seven and three-tenths years, in comparison with an average of ten and two-tenths years reported by Coombs,[10] and seven by Poynton[14] in similarly constituted series. It is important to note that our dating of the age of onset is in all probability accurate because about 50 per cent of the children came under our observation within a year of the onset of their rheumatic infection.

2. *Recurrence of Manifestations of Infection.*—Three hundred and two of 413 children in this group, or 73.0 per cent of the cases, suffered from one or more recurrences of infection (Fig. 5).* This figure must

*Mackie[13] found 71.5 per cent relapses in a series of 252 children, and in a group of 257 cases seen at St. Thomas' Hospital[9] there were 85.0 per cent relapses.

be regarded as a minimum. Attention has already been called to the varying length of time that these children were observed after the first attack of infection. Of the 111 children for whom no recurrence of infection is reported, 53.0 per cent were observed for less than three years after the initial episode, as against only 7.2 per cent observed for less than three years in the series of 302 children for whom relapses are reported. Obviously, before a statement can be

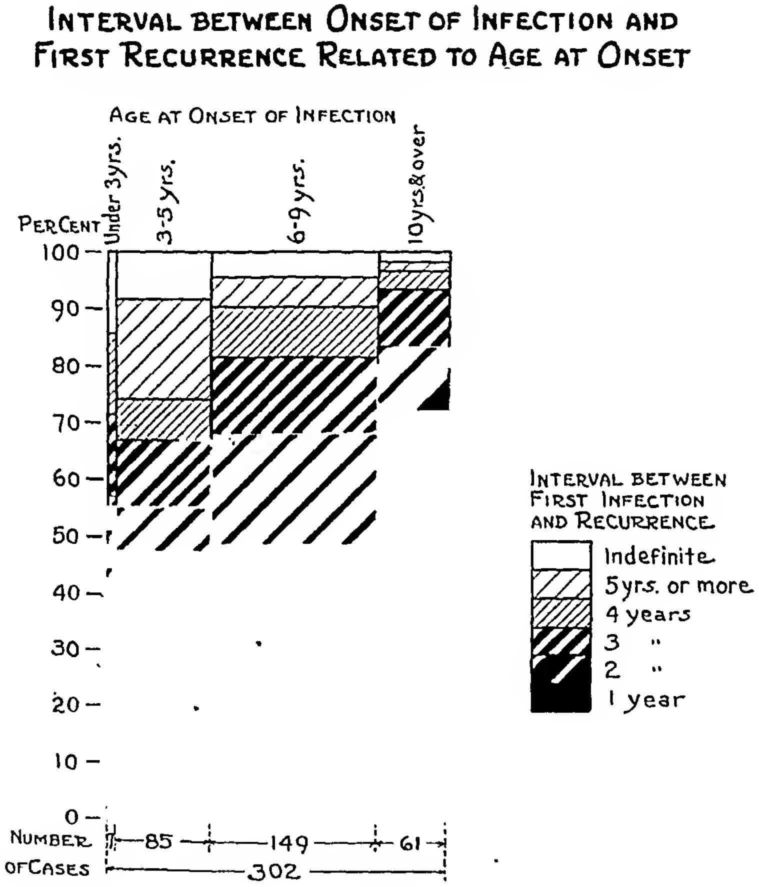

Fig. 5.

made as to the final fate of the 53.0 per cent (those observed less than three years), observation must extend over many more years.

3. *Recurrence of Infection and Age at Onset.*—Recurrences of manifestations of infection during the course of the disease appeared most frequently in the group of children who had acquired their initial infection at an early age. Eighty-five per cent of those who were afflicted between the ages of three and five suffered recurrences, as against 72.3 per cent in whom the initial infection occurred between the ages of six and nine, and 62.8 per cent among those in whom the infection began at ten years or over. Mackie reports the incidence rate of recurrence likewise highest in the group that experienced the

initial attack between the ages of five and ten years. In his series the disease recurred in 93.4 per cent.

4. *Interval Between Onset and Recurrence.*—An analysis of the interval which elapsed between the first noted manifestation of infection and the first recurrence shows that about half of the total cases relapsed within a year, two-thirds within two years, and four-fifths or 80 per cent within three years (Fig. 5). In only 15 per cent did at least four years elapse before the first recurrence of any manifestation of rheumatic infection appeared. There is here a striking difference between our experience and Mackie's, our 50 per cent as against his 23.6 per cent within the first year and our 15 per cent as against his 43 per cent after four or more years. The difference in the age constitution of the two series must again be taken into account. Only 1.4 per cent of our cases, but 48.9 per cent of Mackie's had reached the age of fifteen years or more, when the first rheumatic attack appeared. In our experience, recurrences are most frequent before this age is reached.

When related to the age at onset the greatest incidence of recurrence *within one year of onset* (72.2 per cent) was observed in children who were first infected at the age of ten or more years. This observation is of particular importance because 84 per cent of these children were between ten and twelve years of age, the age of puberty. It is possible that this is a critical age for children with rheumatic infection.

5. *Periods Free From Infection.*—Fig. 6* is a graphic description of the clinical course of the disease experienced by each child. The distribution of the cases† is arranged according to (1) the age at onset, (2) years in which there were manifestations of infection, and (3) the age reached at the time of last observation or report.

Even casual inspection of this chart impresses one with the apparent chronicity of the disease. To experience one, two, three, even four years of freedom from infection is not unusual, but even after longer periods relapses are frequent. Twenty-one children, for example, had 5 consecutive years of freedom from infection. Of these 8, or 38 per cent, relapsed at the end of that time. Thirteen were not under our observation for a longer period, but our experience leads us to expect relapses in some of these, if not in all. For instance, 17 children were free for six consecutive years, of whom 6 relapsed; 6 were free for seven years of whom 4 relapsed; 2 for nine years and one relapsed at the end of that period; of 4 who were free for ten or eleven years, one relapsed even after ten years.

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*For the form of this chart we are indebted to Dr. John Wyckoff who used it in a paper, not yet published, a preliminary report of which was read at a meeting of the Pediatric Section, New York Academy of Medicine, Bulletin of the New York Academy of Medicine, 1926, Second Series, ii, No. 2.

†Case No. 413 was not included in this chart, because dates at which manifestations of infections appeared were not accurately given by child's parent.

Certain detailed considerations disclosed by a study of this chart we desire to discuss.

6. *Age Susceptibility.*—An attempt was made to draw a frequency curve to determine the ages, provided they exist, at which rheumatic subjects are most susceptible to infection. It was found that the 413 children, together, experienced 1728 manifestations of infection, an average of four attacks per child. Because of the difficulty of defining a relapse or recurrence, that is to say, of deciding when one attack has ended and another has begun, it was thought best to present the data according to age at which manifestations of infection occurred, without attempting to determine whether, for instance, a child suffered one or more manifestations in a single year, or whether the second or third manifestation of infection might be but an exacerbation of the original attack. Presentation of the data in this manner shows that the 413 children together experienced 1140 years in which infection was present, an average of two and three-quarters years per child.

The curve showing the ages at which infection was present, when smoothed, appears nearly symmetrical, though somewhat scewed to the right, with a modal average at nine years (Fig. 7-A). The second half of this curve may not represent the facts as they really are because of the relatively small number of children included in this study who reached the upper ages, from nine to sixteen years. Consecutive curves were therefore drawn including data concerning children all of whom reached certain specific ages, as, nine years, ten years and so on, to eighteen. It should be noted from this series of curves that the modal average ranges from nine to twelve years. In every case the curve begins to descend at some point within these age limits. In general, all the curves which succeed it conform to the total frequency curve. The very small number of children that reached the ages of sixteen, seventeen and eighteen years may very likely be responsible for the apparent flatness of these curves to the right of the mode. In spite of the insufficient number of cases included in this series, the curves confirm the belief that rheumatic infection, in its various manifestations, concerns itself primarily with children of the grade school age; their plain meaning seems to be *that about or before the age of twelve, the tendency to infection begins to diminish.*

It seems to us to be of very great importance to point out the probability these curves show, that age may be a factor in judging the influence of any therapeutic measures on the natural course of the infection. The results of any therapeutic measure, such as tonsillectomy, prolonged convalescent care, or specific serum or vaccine therapy instituted before or after children have reached an age of from nine to twelve years, must be judged accordingly. In a subsequent communication a study of the influence of tonsillectomy will be presented in connection with this series of rheumatic children.

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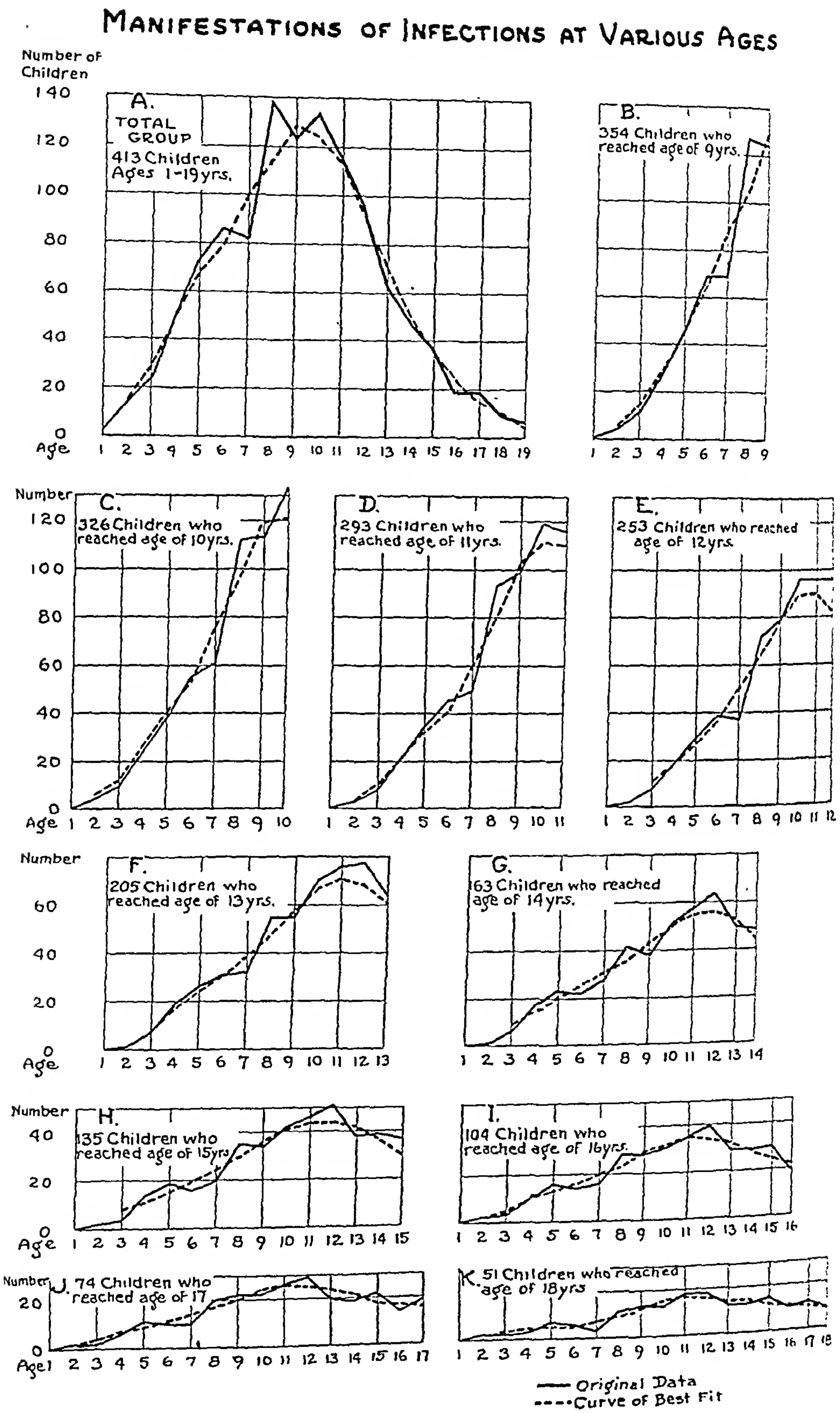

MANIFESTATIONS OF INFECTIONS AT VARIOUS AGES
Number of Children
A. TOTAL GROUP
413 Children Ages 1-19 yrs.
B. 354 Children who reached age of 9 yrs.
C. 326 Children who reached age of 10 yrs.
D. 293 Children who reached age of 11 yrs.
E. 253 Children who reached age of 12 yrs.
F. 205 Children who reached age of 13 yrs.
G. 163 Children who reached age of 14 yrs.
H. 135 Children who reached age of 15 yrs.
I. 104 Children who reached age of 16 yrs.
J. 74 Children who reached age of 17
K. 51 Children who reached age of 18 yrs
Number
Age
Original Data
Curve of Best Fit

Fig. 7.

7. *Expectancy.*—Figures such as these, if they cover a large enough number of cases to satisfy the law of probability, should enable one to draw a curve which would show expectancy at each age; that is to say, would make possible prognostication as to whether a child is likely to have years free from infection immediately following a given age, and if so, how many such years may be expected to pass before a relapse takes place. We have attempted to draw such curves.

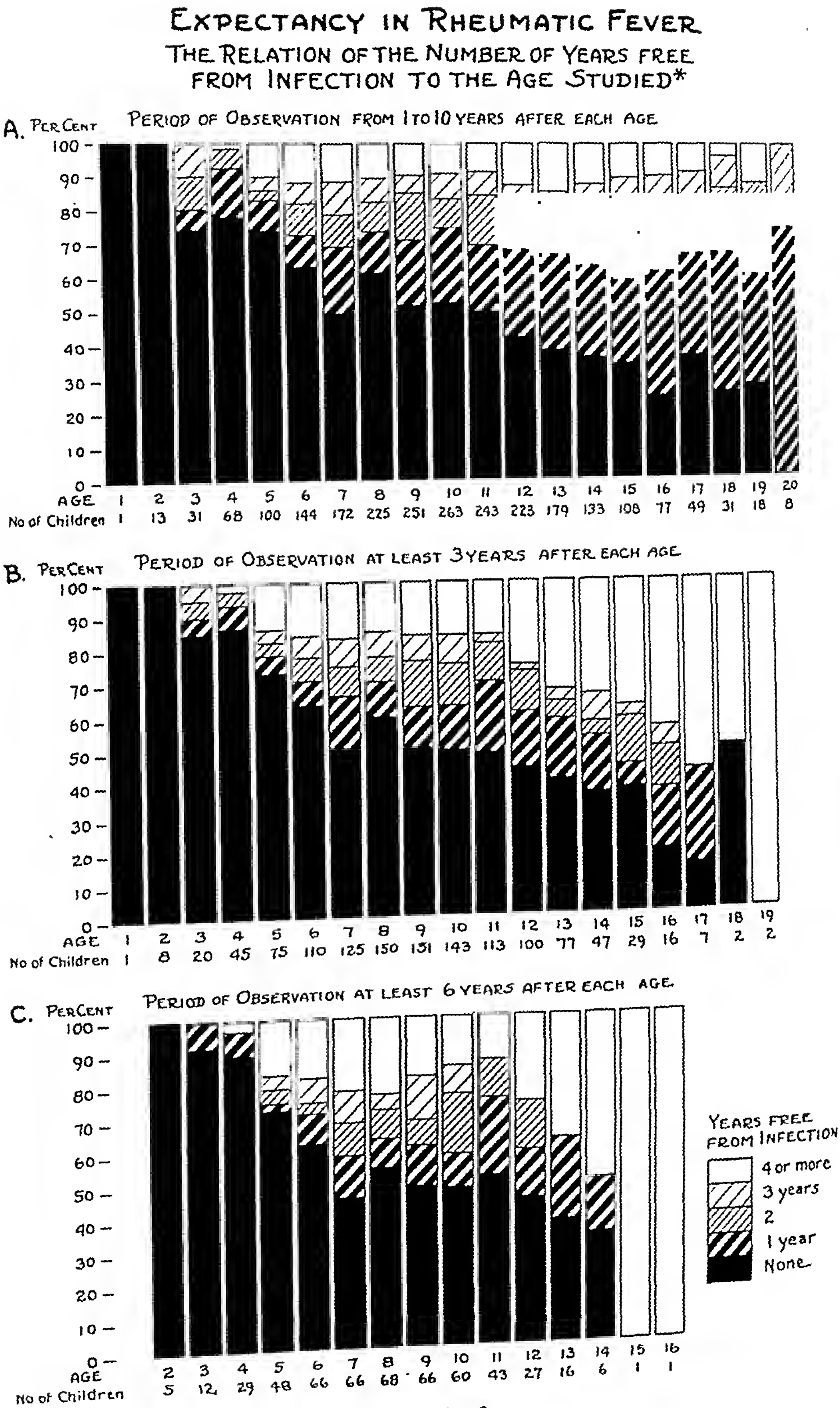
It appears, Fig. 8-A, that there is variation in the number of years that may occur free from infection. Our chart is to be read as follows: Of the 172 children who were infected at or before the age of seven years, 50 per cent relapsed in the eighth year, almost 20 per cent were free from infection in the eighth year, and then relapsed; the remaining 30 per cent were free in the eighth and ninth years, or longer, before relapse took place. Of those who were infected at or before the age of fifteen, however, only 34 per cent relapsed in the sixteenth year; 24 per cent were free in the sixteenth year, and then relapsed, and the remaining 42 per cent were free the sixteenth and seventeenth years, or longer, before relapse took place.

On the basis of this limited experience of 413 cases, one might say, then, that at the age of seven, the chances are even that a rheumatic child will undergo a recurrence the following year; of the children not likely to relapse the following year, the chances are two to three that the interval of freedom from infection will be not greater than one year. At the age of fifteen, however, the chances are only one to three that infection will recur in the following year; if no recurrence takes place at that time, the chances are about one to two that the interval of freedom from infection will be only one year.

The conclusion that can be drawn from this chart may be paraphrased also in this manner; of 172 children who have arrived at the age of seven years, and who have by this time become infected, only 6, or 3.5 per cent, in our experience can hope, in the years following, to remain free from infection for a period as long even as six years; only one for a period as long as ten years. Beyond this our observations do not yet reach.

The older the age group which is studied, the greater seems to be the chance of freedom from infection. At the age of twenty years about 75 per cent were free in the twenty-first year—that is to say, for the next year; and 25 per cent were free for three years, from ages twenty-one to twenty-four. Our records go no further. In comparison with age seven this is a gain, for of these only 50 per cent could hope for one free year, and only about 10 per cent for three such years.

In general, the curves indicate that, at any age before the age of seven, the chances are 3 to 5, or greater, that a rheumatic child will



EXPECTANCY IN RHEUMATIC FEVER
THE RELATION OF THE NUMBER OF YEARS FREE FROM INFECTION TO THE AGE STUDIED*
A. PER CENT
PERIOD OF OBSERVATION FROM 1 TO 10 YEARS AFTER EACH AGE
100 90 80 70 60 50 40 30 20 10 0
AGE 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
No of Children 1 13 31 68 100 144 172 225 251 263 243 223 179 133 108 77 49 31 18 8
B. PER CENT
PERIOD OF OBSERVATION AT LEAST 3 YEARS AFTER EACH AGE
100 90 80 70 60 50 40 30 20 10 0
AGE 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
No of Children 1 8 20 45 75 110 125 150 151 143 113 100 77 47 29 16 7 2 2
C. PER CENT
PERIOD OF OBSERVATION AT LEAST 6 YEARS AFTER EACH AGE
100 90 80 70 60 50 40 30 20 10 0
AGE 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
No of Children 5 12 29 48 66 66 68 66 60 43 27 16 6 1 1
YEARS FREE FROM INFECTION
4 or more
3 years
2
1 year
None

Fig. 8.

be subject to recurrent manifestations of infection the following year; at any age between the ages of seven and eleven, inclusive, the chances are about even, and at any age after the age of twelve, the chances are about 2 to 5. or less. Similarly, the number of consecutive years of freedom from infection tends to increase as the adolescent ages are reached.

It was thought that the fact of the varying number of years that children were observed after different ages might lead to erroneous conclusions. Data were tabulated therefore concerning only those

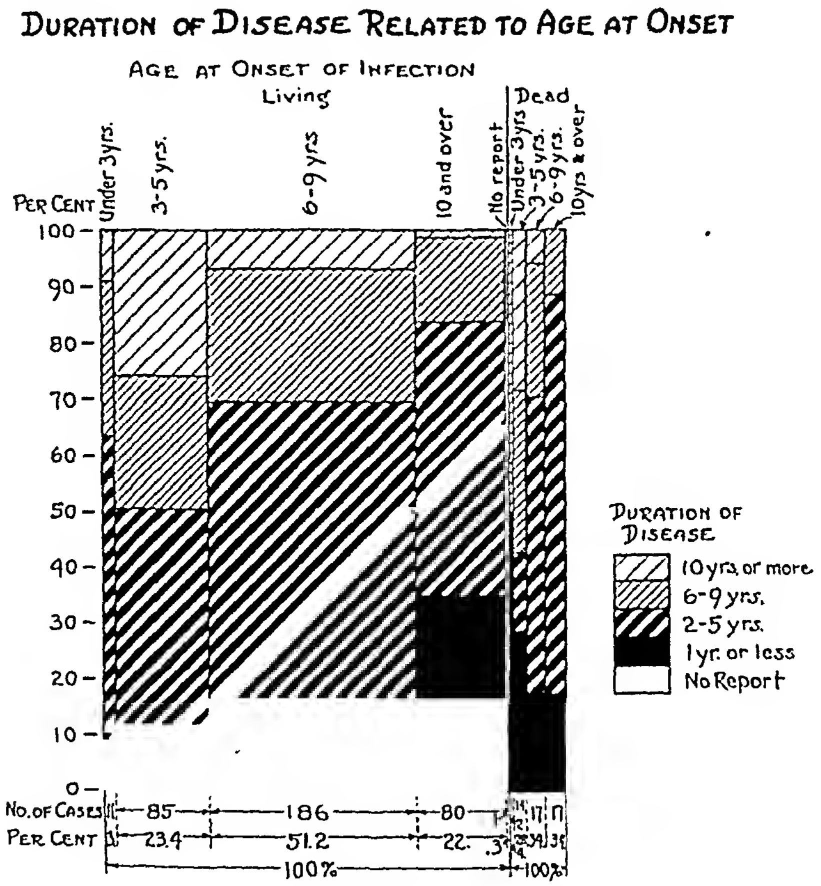


Fig. 9.

children who were observed three years or more (Fig. 8-*B*) or six years or more (Fig. 8-*C*), respectively, that is to say for periods not less than three or six years, after each age. In general, the picture remained the same.

Within recent years, efforts have been made to estimate the results of certain therapeutic measures. Among criteria suggested for making such judgments that of considering recurrences of manifestations of infection after therapeutic measures have been instituted has been emphasized, such therapeutic measures for instance as tonsillectomy or convalescent care. That such judgments cannot confidently be

made without relation to the natural course of the disease, especially without regard to recurrences, seems obvious in view of the data (Figs. 7 and 8) that have been presented.

It must be emphasized again that these curves are not presented as reliable expectancy curves, but merely as preliminary statements based on the facts which have emerged in studying this series of 413 rheumatic children. It is believed, however, that by concerted effort it may be possible later to draw reliable expectancy curves which will be valuable as a background against which to measure results of treatment.

8. *Duration of the Disease.*—Of the total 413 children, 46 per cent came under observation within one year of the onset of the first manifestation of infection. Three hundred and sixty-three, or 88 per cent, are living (Fig. 9). In 67.8 per cent of these the duration of the disease has been from one to five years, in 21.8 per cent from six to nine years, and in 10.2 per cent from ten to sixteen years. Fifty children, or 12 per cent died. Eleven, or 22 per cent, died within one year of the onset of infection. In 46 per cent the duration of the disease was from six to nine years, and in 10 per cent from ten to fifteen years.

9. *Prognosis.*—From the data presented, little of prognostic value could be learned. This may be due to the fact that the number of deaths is small, even though the mortality rate in the series is relatively high. When the age at death was compared with the age distribution of the living, it was found that no single age or age group claimed a predominatingly high mortality. Likewise, there appeared to be no relation between mortality and the duration of the disease. The age at onset, however, and the severity of a particular attack of infection appeared to influence the duration of the disease. The figures indicate that children infected before the age of five and after the age of ten have a somewhat less favorable prognosis than those infected in the intermediate ages.

10. *Causes of Death.*—In forty-four children, or 88 per cent of the deaths, the cause of death was rheumatic heart disease. Death followed acute rheumatic carditis in 34 of these. One child died of bacterial endocarditis, one of lobar pneumonia, one of suppurative appendicitis, one of miliary tuberculosis, and two of causes unknown. The most common age at death was between eleven and fourteen years. Forty-five per cent of the deaths occurred in this age group.

11. *Incidence of Measles and Scarlet Fever.*—The possible relation between susceptibility to rheumatic and to other infections was considered. Two hundred and twenty-two, or 53.7 per cent, of the rheumatic children presented a history of measles. In 36.9 per cent, measles occurred between the ages of three and five years (Table III).

Halsey[15] found that the incidence of measles in cardiac children was 36 per cent, and in noncardiac children in certain public schools in New York City was 58 per cent. Among a thousand newsboys recently examined in New York City, 34 per cent reported a history of measles.[16]

Scarlet fever occurred in 42, or 10.2 per cent, of the rheumatic children, as compared with 12 per cent in the cardiac and 5 per cent in the noncardiac children in Halsey's series. Among the newsboys referred to above, 5.6 per cent reported a history of scarlet fever. Coombs[10] has referred to the significance of scarlet fever as a precursor of rheumatic heart disease. Hector[17] suggests that "the almost invariable result of scarlet fever upon the heart already damaged by rheumatism may be a rekindling of the old affection which in some cases had been quiescent for a considerable period, and that a mild or moderate attack of scarlet fever is quite capable of bringing this about." It is interesting to note, that like the various manifestations of rheumatism, and unlike measles and tonsillitis, scarlet fever occurred most often, in 38.3 per cent of the cases, between the ages of

TABLE III

INCIDENCE OF MEASLES AND SCARLET FEVER BY AGE GROUPS

AGE IN YEARS	MEASLES		SCARLET FEVER	
	NO.	PER CENT	NO.	PER CENT
Under 3	54	24.3	6	14.2
3 to 5	82	36.9	11	26.2
6 to 9	49	22.2	16	38.3
10 and over	2	0.9	6	14.2
Unknown	35	15.7	3	7.1
Total	222	100.0	42	100.0

six and nine years (Table III). Fig. 10 shows the chronological relation of scarlet fever to manifestations of rheumatic infection. In 21, or 54.3 per cent, of the cases it preceded a rheumatic manifestation; in 6, or 15.4 per cent, it occurred in the same year with the first manifestation of rheumatic infection, and in 12, or 30.7 per cent, it followed a rheumatic manifestation.

The age incidence of scarlet fever as reported in 3940 cases seen in the Willard Parker Hospital in the years 1919 to 1923, inclusive, is highest (31.8 per cent) between the ages of six and ten, and (25.4 per cent) between the ages of three and five.[18] That is to say, the age incidence of scarlet fever is similar to that of rheumatic infection. The common association of polyarthritis and chorea with scarlet fever may be due to this factor.

12. *Relative Incidence of Various Manifestations.*—An analysis of 413 case records which form the basis of this report shows the incidence of manifestations of rheumatic infection to be as follows:

A. *Polyarthritis* was the most frequent major manifestation noted, occurring from one to six times or more in each of 272 children, 65.8

per cent (Fig. 11). It was the most common manifestation found at onset, occurring in 169 children, or 40.9 per cent (Fig. 3). As a first manifestation of infection it appeared most frequently between the ages of six and nine years, in 41.4 per cent of the children. In 30.8 per cent it occurred between the ages of three and five. It occurred as a first manifestation under three years of age in only 9 children.

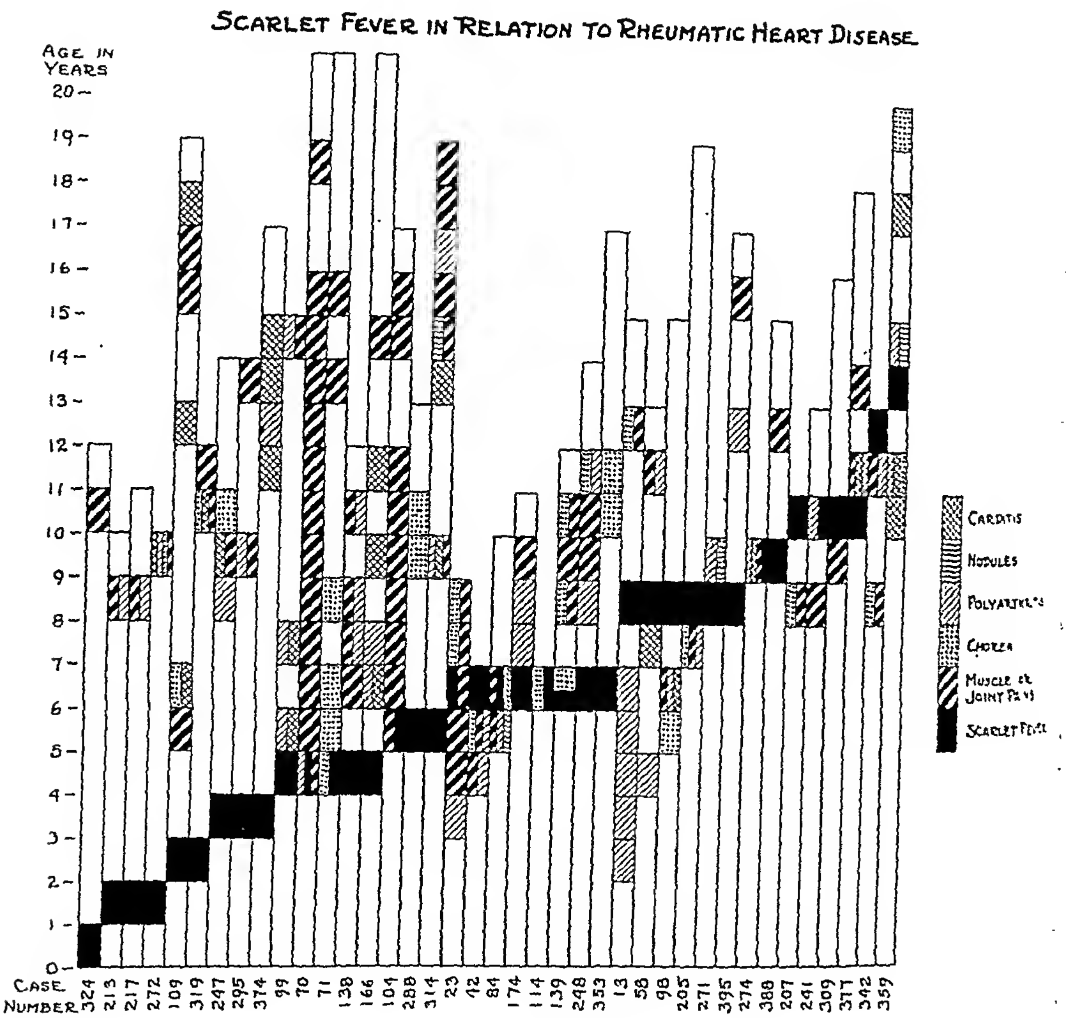


Fig. 10.

B. *Growing and Joint Pains* occurred in each of 278 children, or 67 per cent (Table IV). As the first manifestation of infection they occurred in 26.6 per cent. In more than half the children, 53.6 per cent, they occurred, like polyarthritis, as a first manifestation, between the ages of six and nine (Fig. 3). In 64 cases, or 23 per cent, they preceded the so-called major manifestations, chiefly polyarthritis. In half of these, major manifestations of infection followed within a year; in almost three-quarters within three years. In 10.9 per cent growing and joint pains were followed by acute carditis without any inter-

vening manifestation of polyarthritis or chorea (Table V). In 81 cases, or 29 per cent, they occurred after other manifestations, and in 87 cases, or 31.3 per cent, they occurred in the same year with, but were dissociated from, the major manifestation—polyarthritis, chorea, or carditis. In 46 children growing and joint pains were the only manifestations of rheumatic infection, except one or more attacks of tonsillitis in half the cases. In all but four of these 46 children there was some heart involvement. Only four had no evidence of heart disease when last seen. (Table IV.)

TABLE IV

MUSCLE AND JOINT PAINS RELATED TO OTHER RHEUMATIC MANIFESTATIONS

MUSCLE OR JOINT PAINS		TOTAL CHILDREN	
		NUMBER	PER CENT
Without other rheumatic manifestations		46	16.5
Preceding	Other rheumatic manifestations	64	23.1
Same year with	Other rheumatic manifestations	87	31.2
Following	Other rheumatic manifestations	81	29.2
Total		278	100.0

TABLE V

INTERVAL BETWEEN EARLIEST SYMPTOMS OF MUSCLE OR JOINT PAINS AND FIRST DEFINITE MANIFESTATION OF RHEUMATIC FEVER

JOINT PAINS PRECEDING RHEUMATIC MANIFESTATION	% OF TOTAL	TOTAL		INTERVAL IN YEARS					
				LESS THAN 1 YR.		1 TO 2 YR.		3 TO 5 YR.	
		NO.	%	NO.	%	NO.	%	NO.	%
Joint Pains Preceding Polyarthritis	67.2	43	100	23	53.5	11	25.6	9	20.9
Joint Pains Preceding Chorea	21.9	14	100	4	28.6	3	21.4	7	50.0
Joint Pains Preceding Carditis	10.9	7	100	5	71.4	1	14.3	1	14.3
Total	100.0	64	100	32	50.0	15	23.4	17	26.6

Growing and joint pains are usually recognized as minor manifestations of rheumatic infection. We believe, however, that their significance has been underestimated. It has been previously shown[19] that growing and joint pains are a manifestation of activity of the infection as judged by curves of the leucocyte count. We believe that the data presented concerning the age incidence, relative frequency of recurrence, and associated heart involvement should place growing and joint pains as a manifestation of equal significance with polyarthritis and chorea.

C. *Tonsillitis* occurred in one or more attacks in 199, or 48.2 per cent, of the children (Fig. 11). Two hundred and fourteen did not give a history of tonsillitis. As a first infection it occurred in 59, or 14.3 per cent, of the cases, the age distribution being from six to

nine years in 32.2 per cent; from three to five years in 30.5 per cent, and under three years in 28.8 per cent (Fig. 3).

D. *Chorea* occurred in one or more attacks in 177 children, or 42.8 per cent (Fig. 11). The sex distribution, contrary to expectation, did not show any striking predominance, occurring in 63.0 or 39.6 per cent of the boys and in 114 or 44.9 per cent of the girls (Fig. 12). In 14.8 per cent, or 25 children, chorea was the sole manifestation, but in only 5 of these was the heart apparently normal. As a manifestation of the first infection it occurred in 86 children, or 20.8 per cent, the most common age being, again, between six and nine years (55.7 per cent).

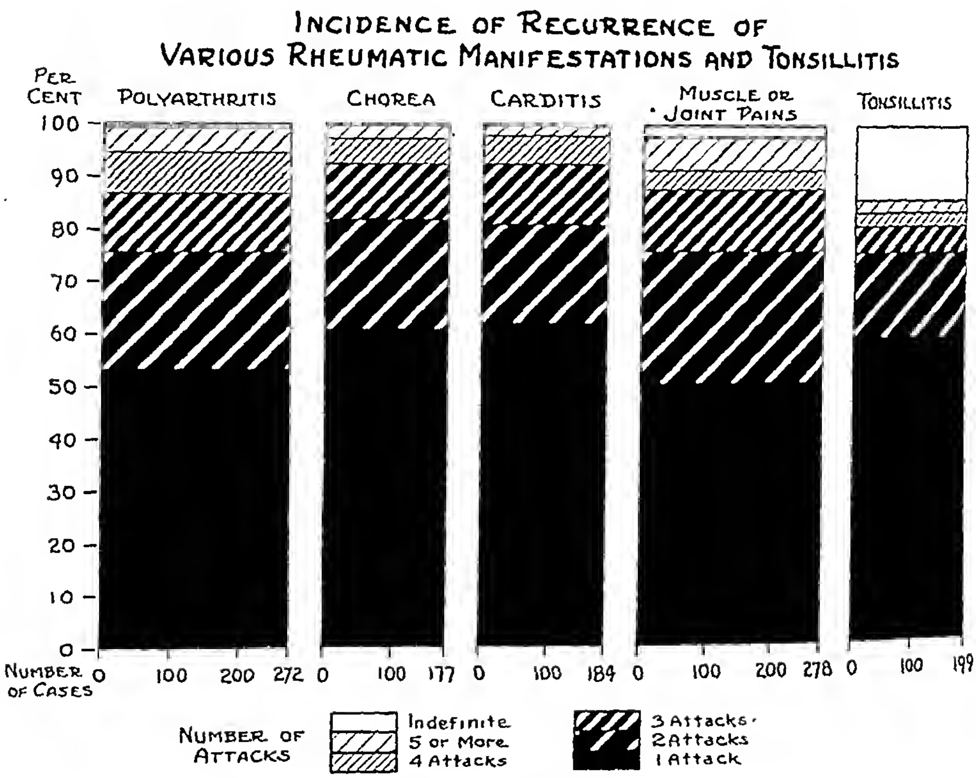


Fig. 11.

As a first manifestation of infection, chorea occurred less frequently before the age of six and more frequently after the age of ten, than any other rheumatic manifestation (Fig. 3).

E. *Nodules* were observed in 60 patients, or 14.5 per cent (Fig. 13). In 43.3 per cent of these they appeared between the ages of six and nine years, and in an equal number, after the age of nine (Fig. 14). In only eight cases did they appear under the age of five years. Twenty, or 33.3 per cent, of the children who presented nodules died, and 40, or 66.6 per cent, are living. Of those who died 60 per cent expired within one year and 80 per cent within three years after nodules were first observed. Of those still living, 45 per cent are living three or more years after nodules were first observed. Nodules occurred toward the

end of periods of active infection. They were associated, as a rule, with other severe manifestations. They appeared in three cases in which no evidence of rheumatic heart involvement has so far been observed. Twelve patients presented only mitral insufficiency, and forty-three presented severe heart involvement (Fig. 14). In a comparable series of 172 children under the age of twelve, Poynton[14] found nodules in 19 per cent. Our experience leads us to believe that nodules are not less common in the United States than in England.

F. *Rheumatic Heart Involvement.*—One hundred eighty-four children, or 44.5 per cent, either gave a history of acute rheumatic carditis or presented an attack while under observation. One hundred and fourteen of these, or 62 per cent, experienced one attack; 35, or 19.0

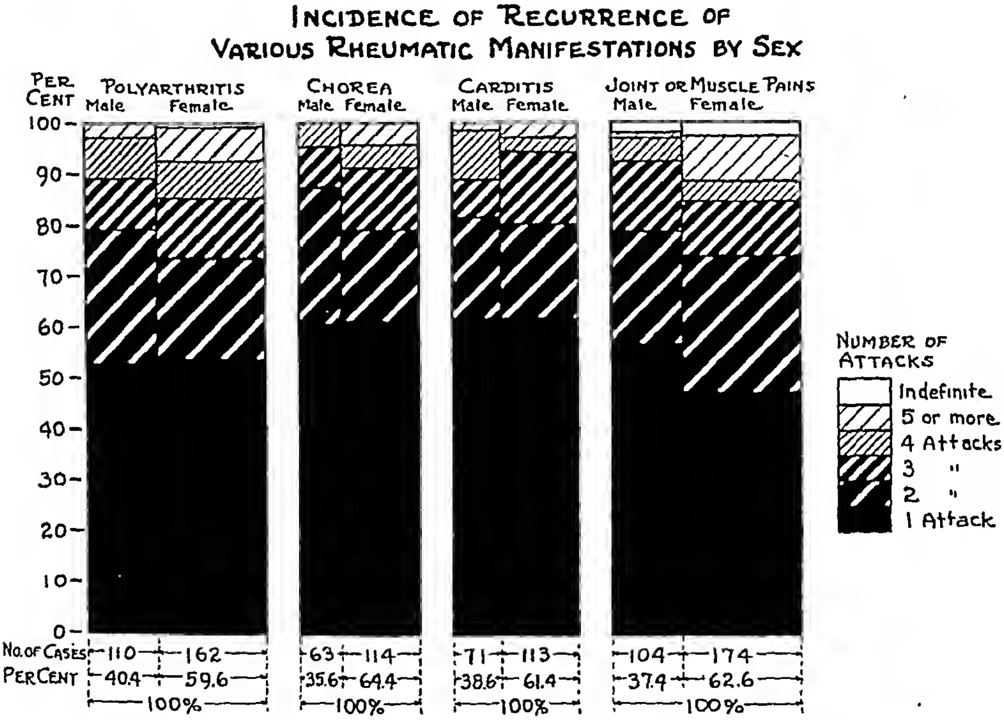


Fig. 12.

per cent, two attacks; and 35, or 19.0 per cent, three or more attacks* (Fig. 11). As a manifestation of first infection it was noted in 6.3 per cent of the cases. As a first manifestation it occurred most frequently between the ages of six and nine years, as did the other manifestations of rheumatic infection. Ten children presented at least one attack of carditis, and no other rheumatic manifestation. The symptoms of acute rheumatic carditis were frequently so slight as almost to escape detection. One hundred and twenty-eight children with rheumatic heart† disease did not give a history of any symptoms of acute

*The use of the term acute rheumatic carditis includes acute rheumatic myocarditis, endocarditis, and pericarditis.

†These observations are in accord with the common experience of discovering definite organic heart disease in older children and adults without a history of previous relative illness.

carditis (Table VII). Thirty-five developed definite heart disease while under our observation and did not present symptoms of acute carditis—the heart enlargement and the valvular lesion developing insidiously. Symptoms of congestive heart failure with edema occurred in 9 children and ended fatally in 6 cases.

Three hundred and twenty-eight, or 79.5 per cent, exhibited rheumatic heart involvement. The approximate age at onset of heart disease could be ascertained in 252 cases. In 76 the age given is doubtful.* The age at onset of the heart involvement, in the 252 cases, was between six and nine years in 45.6 per cent (Table VI).

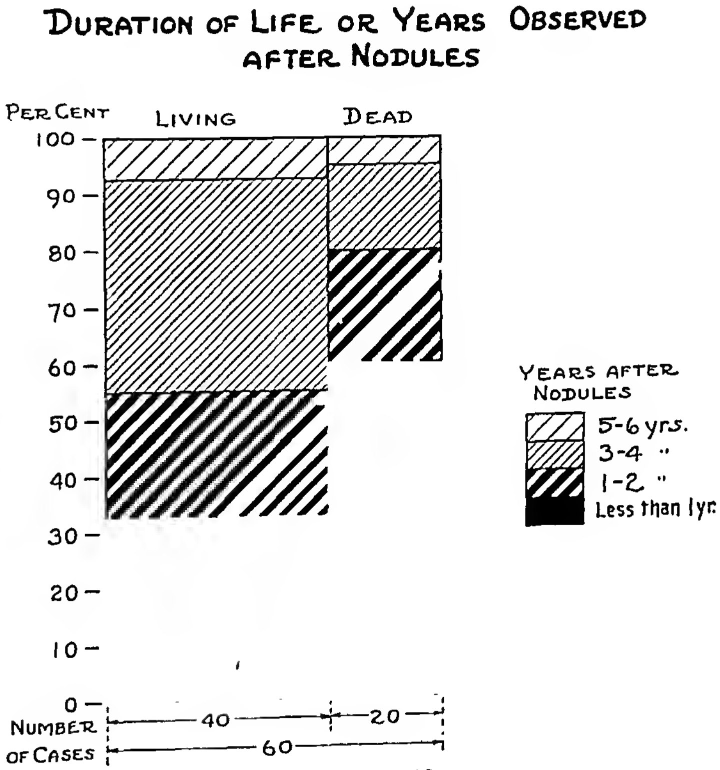


Fig. 13.

In the 76 cases in which the age at onset was doubtful, it was reported as between six and nine years in 39.5 per cent. The interval between the first manifestation of rheumatic infection and heart involvement in the 252 cases was one year or less in 63.1 per cent.† This is in marked contrast to Cohn's[1] statistics based on available published data, namely, that the interval between the beginning of infection and the establishment of chronic cardiovalvular disease ranged from one to eight years, with an average of four years.

*Where the age of onset of heart involvement was not observed but taken from the history record, the age was regarded as doubtful unless the symptoms given were characteristic.

†Mackie reports serious cardiac involvement in 68 per cent of cases, irrespective of age; an incidence of heart disease in the first attack of rheumatic fever in 61.5 per cent, of all cases under the age of five, in 78.1 per cent of cases between the ages of five and ten, and in 79.2 per cent of cases between the ages of ten and fifteen."

TABLE VI

INTERVAL BETWEEN ONSET OF INFECTION AND CARDIAC INVOLVEMENT RELATED TO AGE AT ONSET OF INFECTION

AGE IN YEARS AT ONSET OF INFECTION	PER CENT OF TOTAL	TOTAL		INTERVAL BETWEEN FIRST INFECTION AND CARDIAC INVOLVEMENT											
				LESS THAN 1 YEAR		1 TO 3 YEARS		3 TO 5 YEARS		6 TO 9 YEARS		10 YEARS OR MORE		UNKNOWN	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Under 3	4.0	10	100	7	70.0	0		3	30.0	0		0			
3 to 5	26.6	67	100	39	58.3	7	10.4	15	22.4	6	8.9				
6 to 9	45.6	115	100	80	69.5	19	16.5	13	11.3	3	2.6				
10 or over	14.7	37	100	33	89.2	2	5.4	2	5.4						
No record	9.1	23	100											23	100.0
Total	100.0	252	100	159	63.1	28	11.1	33	13.1	9	3.6	0		23	9.1

When related to the age at onset of infection, it appeared that the interval between initial infection and heart involvement decreased as the age at which the child became infected increased. This was not so in the case of children infected before the age of three. Since there were only 10 children in this group, it is probable, however, that the figures are too small to be significant.

13. *Potential Heart Disease.*—Of 159 children who on admission were classified as cases of "potential heart disease,"* the heart was normal

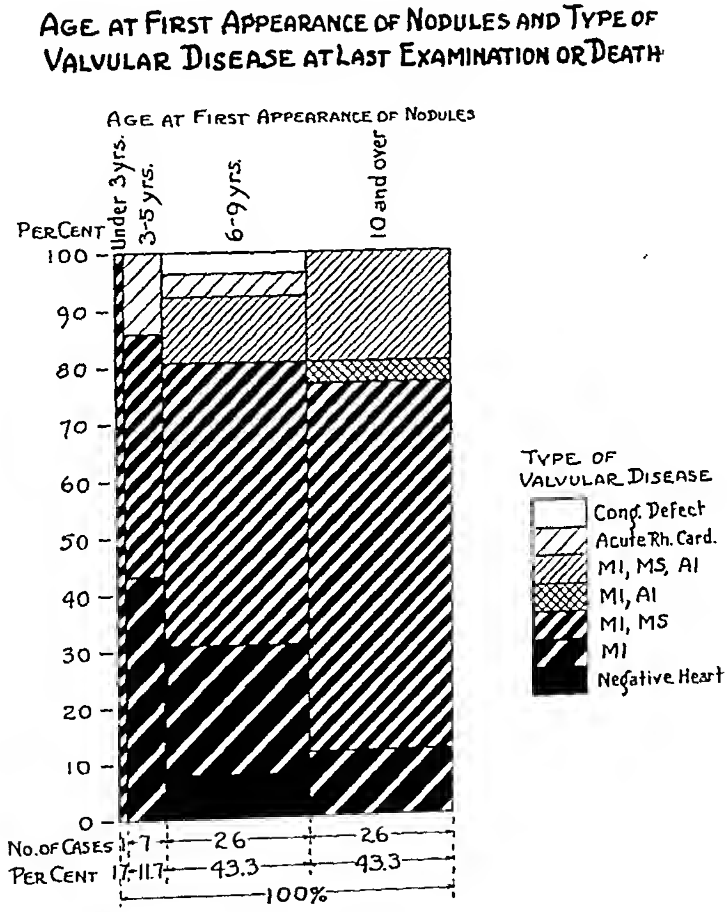


Fig. 14.

in 72, or 45.2 per cent; in 60, or 37.7 per cent, the heart was enlarged; in 11, or 6.9 per cent, a systolic murmur was present but not constant, and in 16, or 10.0 per cent, the heart was enlarged and an inconstant systolic murmur was present. Fifty-nine, or 37.1 per cent, developed definite valvular lesions; 98, or 61.6 per cent, remained in the "potential" group. Of these, 25 remained apparently normal; in 43, or 27.9 per cent, the heart became enlarged; in 6 an inconstant systolic murmur was heard, and in 24 there appeared both enlargement and an

*Potential heart disease, Class F, classification of the American Heart Association. Patients without circulatory disease whom it is advisable to follow because of the presence or history of an etiological factor which might cause disease.

inconstant murmur. Five children who on admission were believed to present mitral lesions were placed in the "potential" group on final examination (Table II). If the evidence of enlargement and an evanescent murmur noted in children in the "potential" group may be considered as evidence of some rheumatic heart involvement, then the incidence of heart involvement in the 413 children with rheumatic infection would be about 91 per cent in this group. Swift[21] observed electrocardiographic evidence of some degree of functional cardiac dis-

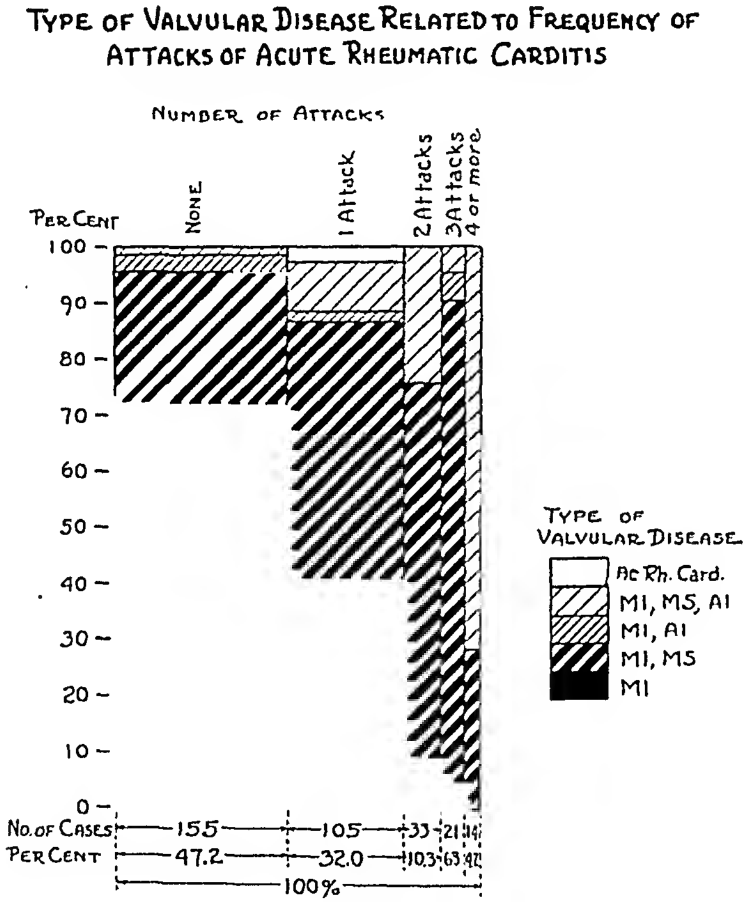


Fig. 15.

turbance in over 90 per cent of a series of 81 patients suffering from rheumatic fever. What the actual incidence of rheumatic heart involvement is, in any series of observations, depends naturally on the method of examination and the criteria used. Slight but insignificant changes in physical signs may be overlooked unless children are under constant and careful observation.

14. *Cardiac Valvular Disease.*—Three hundred and twenty-eight children presented clinical evidence of valvular heart disease. Of these, a diagnosis of mitral insufficiency was made in 48.5 per cent, mitral stenosis and insufficiency in 39.6 per cent, and aortic and mitral

disease* in 10.9 per cent. (Fig. 15.) Of 157 children who were believed to present mitral insufficiency on admission, 48 developed mitral stenosis—14 within three years, and 34 after three or more years. One developed aortic insufficiency, and 2 developed both mitral stenosis and aortic insufficiency; in 2 the heart remained enlarged, but the murmur disappeared; in 2, both the enlargement and murmur disappeared, and in one only a systolic murmur without enlargement was present when last seen. On final observation 101 remained with signs of mitral insufficiency (Table II).

The incidence of single or multiple valvular lesions seemed to be related to the number of attacks of carditis.

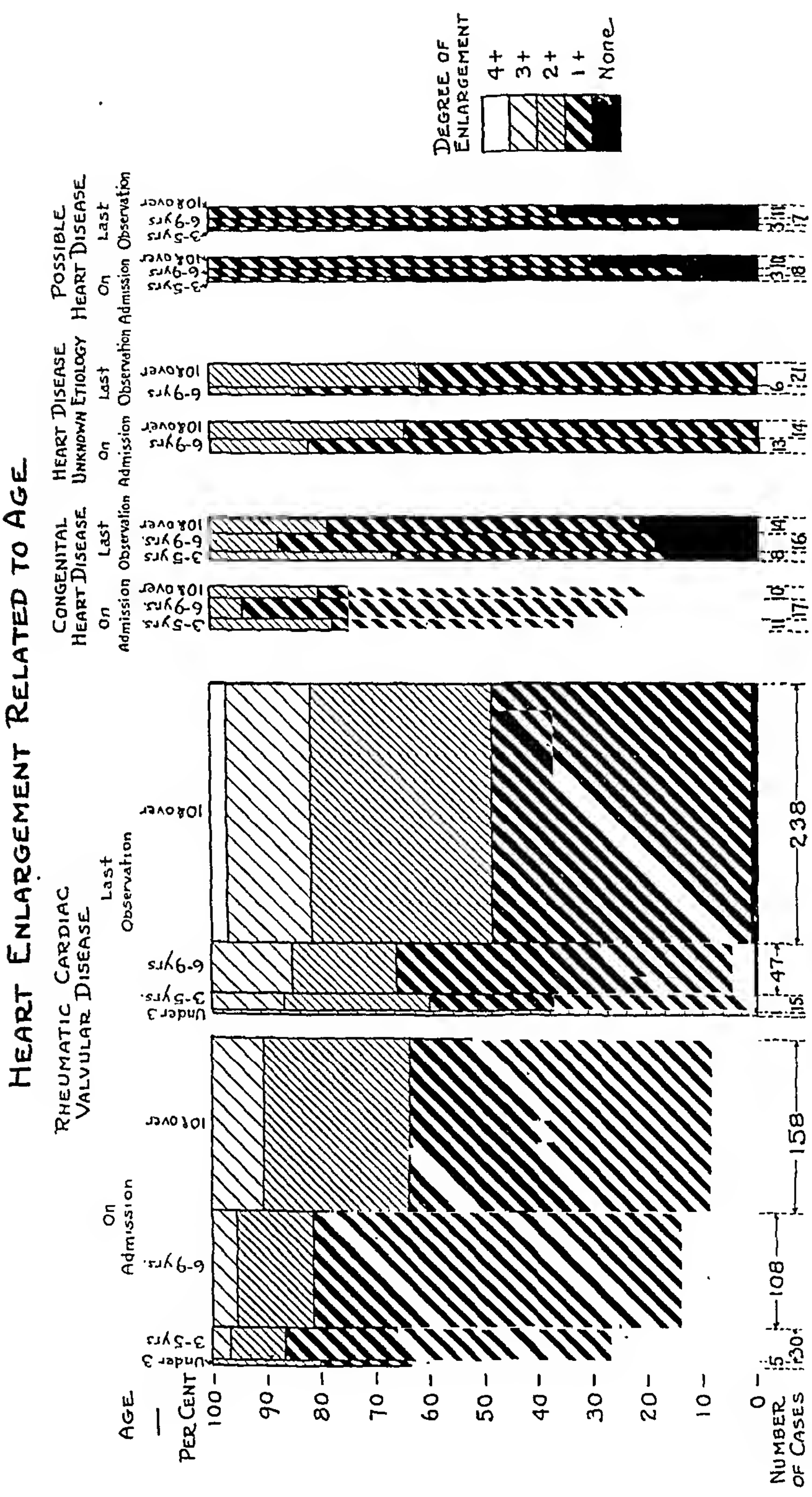
15. *Multiple Valvular Lesions Related to Attacks of Carditis.*—The incidence of multiple valvular lesions was greatest in children who experienced four attacks of carditis. In children who experienced two or three attacks of carditis, mitral stenosis with insufficiency was the most common lesion. The incidence of single lesions (mitral insufficiency) was most frequent in children having but one or no recognized attack of carditis (Fig. 15). A single attack was followed by mitral insufficiency in a very large number of individuals (41 per cent). This observation tends to confirm the view that cardiac involvement is a very frequent concomitant of rheumatic fever.

A comparison of the incidence of mitral stenosis in 125 children with a history of chorea, and in 176 children with a rheumatic history exclusive of chorea, showed practically no difference. If anything, mitral stenosis occurred more often in the group that had not had chorea.

16. *Heart Enlargement.*—On final observation 150 children, or 49.8 per cent of the children who were afflicted with rheumatic heart disease, showed slight heart (1+) enlargement. Ninety-two, or 30.6 per cent, showed moderate heart enlargement (2+), and 53, or 17.6 per cent, showed marked enlargement† (3+, 4+, etc.). (See Table VII.) A comparison of the size of the heart with the age of the child at the time of first and last observation shows a slight increase in size at the later date. A similar comparison of the size of the heart of children suffering from congenital heart disease, heart disease of unknown etiology, or "possible" heart disease, on first and last observation, showed no appreciable difference (Fig. 16). These observations seem to indicate that changes in the size of the heart are not related to age. A comparison of the size of the heart with the number of attacks of carditis shows an increased incidence of three-plus enlargements in

*The diagnostic criteria of the Heart Committee, New York Tuberculosis and Health Association were adhered to.[20]

†The size of the heart was arbitrarily graded one to four plus, the diagnosis being made by routine serial fluoroscopic tracings checked in questionable cases by teleoroentgenograms.



Heart Enlargement Related to Age
Rheumatic Cardiac Valvular Disease
On Admission
Last Observation
Congenital Heart Disease
Heart Disease Unknown Etiology
Possible Heart Disease
Age
Per Cent
Under 3
3-5 yrs.
6-9 yrs.
10 & over
100
90
80
70
60
50
40
30
20
10
0
Number of Cases
5
30
108
158
15
47
238
Degree of Enlargement
4+
3+
2+
1+
None

Fig. 16.

TABLE VII

HEART ENLARGEMENT IN RELATION TO NUMBER OF ATTACKS OF CARDITIS IN 301 CASES OF RHEUMATIC HEART DISEASE

CARDITIS	% OF TOTAL	TOTAL		DEGREE OF ENLARGEMENT											
				1+		2+		3+		4+		NONE		UNDETERMINED	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
1 attack	34.8	105	100	43	40.9	40	38.1	17	16.2	1	1.0	1	1.0	3	2.8
2 attacks	11.0	33	100	6	18.2	12	36.4	11	33.3	4	12.1	0		0	
3 attacks	6.9	21	100	4	19.0	8	38.1	8	38.1	1	4.8	0		0	
4 or more attacks	4.6	14	100	1	7.1	3	21.4	9	64.3	1	7.1	0		0	
None	42.7	128	100	96	75.0	29	22.8	1	0.8	0		2	1.4	0	
Total	100.0	301	100	150	49.8	92	30.6	46	15.3	7	2.3	3	1.0	3	1.0

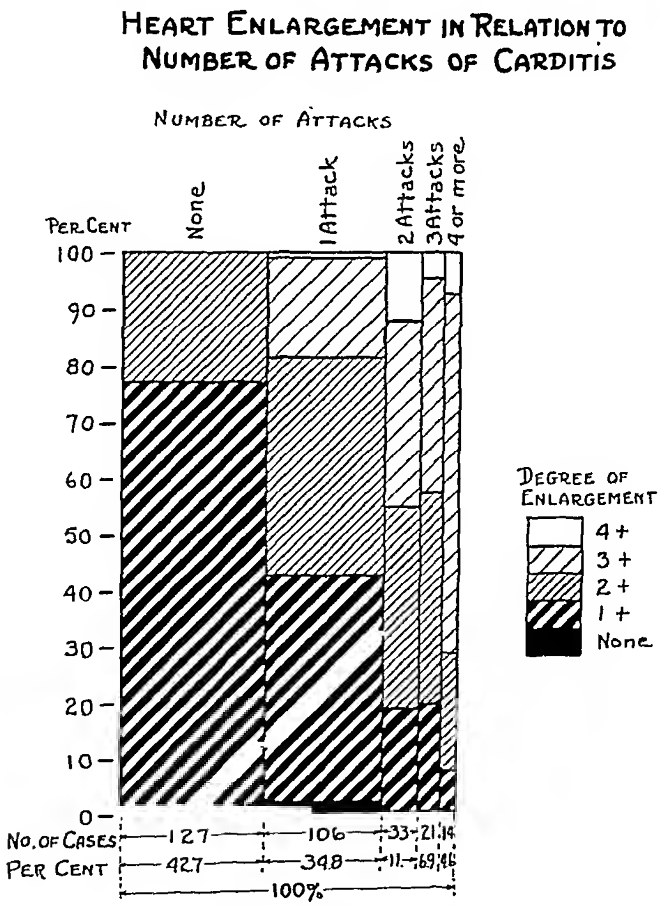


Fig. 17.

children who experienced four or more attacks of carditis (Fig. 17). In our experience, then, the degree of heart involvement, as determined clinically by the size of the heart and the number of valves involved seems closely related to the number of recurrent attacks of acute rheumatic carditis, rather than to the age of the child.

17. *Functional Classification.*—On final observation 313 children with rheumatic heart disease were classified according to functional capac-

ity. Seventy and six-tenths per cent were found to be in Class I; 11.2 per cent in Class IIA; 1.9 per cent in Class IIB, and 13.1 per cent in Class III.[20] These figures indicate that the majority of children with rheumatic heart disease are able to tolerate a normal amount of work and exercise.

18. *Rate and Rhythm.*—Pathological arrhythmias are infrequent in children. In this series 8 children developed auricular fibrillation. All of these cases were fatal. One child with congenital heart disease suffered from repeated attacks of paroxysmal tachycardia.

COMMENT

If it may be assumed that these 500 children observed over a period of ten years comprise a representative sample of children attending a heart clinic in New York City the resulting statistics, although based on a small number, may be taken as indicating the status of heart disease in children of the class and age groups that were studied. Accumulation of such statistics collected in a uniform manner will correct such inaccuracies as may be due to smallness of number or lack of the representativeness of the sample.

From these data it is apparent that rheumatic infection is the most common etiological factor in the causation of heart disease in childhood. The clinical course is in marked contrast to that which obtained in children with nonrheumatic heart involvement. The latter retained the same physical signs, without progression, over a period of years.

A consideration of the data presented on the natural history of rheumatic infection in its relation to heart disease suggests that rheumatic infection as observed in children is a general infection. It attacks mainly children of school age, six to nine years; its course is characterized by frequent periods of activity, these being most frequent during the first three years after onset, and followed by a diminishing number of recurrences. The diminution is particularly noticeable after the age of twelve when what may be called immunity seems to be developing. The ages under three and from ten to fourteen appear to be critical periods of particular vulnerability, as judged by the rate of mortality and by the increased activity of the disease at these age periods.

In this study periods of activity of infection included symptoms of growing and joint pains, polyarthritis, chorea, nodules and acute carditis. Other recognized associated symptoms were not utilized for statistical analysis because it was not believed that such data could be obtained with sufficient accuracy from a history record. Since these manifestations were always associated with the aforementioned symptoms, the exclusion of the former did not appreciably influence the final statistical correlations.

The heart is probably always affected at the onset of this disease, Although, as has been indicated, its involvement is not always detected clinically. In 63 per cent of the cases the interval between the onset of infection and definite heart involvement was one year or less. The extent of the involvement of the heart increased with repeated periods of activity, and seemed to remain the same in quiescent periods. The type of associated manifestation did not seem to be related to the onset or degree of heart damage.

It seems, then, that in children rheumatic infection manifests itself as a general infection in which the heart is probably the first and main seat of involvement, although this fact is often obscured because the associated manifestations appear more prominent, being, as they are, more easily recognized clinically.

Comparison between various statistical studies of rheumatic infection is difficult. Studies which include adults are not always comparable with observations limited to children, nor are those which view rheumatic polyarthritis and chorea as separate clinical entities, with heart disease as a complication, comparable with our conception of rheumatic infection. If the conception which we adopt is valid *the prevention of heart disease in children means the prevention of rheumatic infection.*

In judging the results of therapeutic measures of prevention or control it is necessary to have in mind the influence of age on the course of the disease; that is to say, the influence of age on increasing susceptibility, up to a certain period, and developing immunity.

SUMMARY

1. Of 500 children ranging in age from two to twenty-two years, observed in a heart clinic, four-fifths presented a rheumatic history.

2. Congenital heart defects occurred in 50, or 11.2 per cent. In 18 of these there was subsequent rheumatic infection.

3. Children with "possible heart disease" (systolic murmur heard between the second and fourth left interspaces) retained the same physical signs without progress over a period of years.

4. The average age at onset of rheumatic infection was 7.3 years. In one-half the children the onset occurred between the ages of six and nine years.

5. Rheumatic infection concerns itself primarily with children of the grade-school age; about the age of twelve the tendency to infection begins to diminish.

6. Three-fourths of 413 children with a rheumatic history developed definite heart disease and one-fourth were "potential heart disease" cases.

7. The heart is probably always involved to some extent at the time of the first infection (some evidence of involvement was noted in 91 per cent at the time of last observation), although marked involvement was noted in only 63 per cent within one year of onset.

8. The associated manifestations of rheumatic infection were not indicative of the degree of heart involvement. Growing and joint pains bear the same relation to heart involvement as polyarthritis or chorea.

9. The degree of heart involvement seemed closely related to the number of attacks of carditis.

10. Twelve per cent of the children died. Eighty-eight per cent of the deaths were due to rheumatic heart disease. The most common age at death was between eleven and fourteen years.

11. The earlier the age of onset of infection the greater is the number of recurrences. The later the age at onset the greater is the number of recurrences within one year.

CONCLUSION

Accumulation of statistical data collected in a uniform manner will lead to a better understanding of heart disease in children, particularly rheumatic heart disease.

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STATISTICAL STUDIES BEARING ON PROBLEMS IN THE CLASSIFICATION OF HEART DISEASE

IV. Tonsillectomy in Its Relation to the Prevention of Rheumatic Heart Disease*

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INTRODUCTION

TONSILLECTOMY is an old surgical procedure. Glover[1] states that the tonsils were removed as early as 10 A.D. Today tonsillectomy has become so commonplace that it is almost a routine in childhood.

The function of the tonsil has not been definitely ascertained. Digby[2] believes that the tonsil plays an important function in immunizing the body against pathogenic bacteria. Canfield[3] believes that a child is more susceptible to infection following tonsillectomy and adenoidectomy. This observation is in accord with the clinical experience of many.

Opinions differ concerning signs that are indicative of disease of the tonsils. Coakley‡ suggests that attention be paid to:

1. The distribution of lymphoid tissue of the lingual tonsils, the nasopharynx, nasal mucosa, the posterior pharyngeal wall, the lateral aspect of the pharynx behind the posterior pillars and below the tonsil on the lateral aspect of the pharyngeal wall, and infection of the para-nasal sinuses and mastoid.
2. The so-called "embedded" tonsil.
3. The thin, creamy secretion that comes from the upper portion of the tonsils.
4. The history of repeated attacks of tonsillitis.
5. Injection of the plica and the anterior pillars of the fauces.

The frequent occurrence of tonsillitis or sore throat in children subject to rheumatic infections has suggested that the tonsil is the probable portal of entry and focus of infection. Tonsillitis and sore throat are, however, common complaints and, certainly, in the majority of cases these affections are not followed by the rheumatic cycle. Maclachan[4] believes that the tonsils are probably more fre-

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†Working on behalf of the Research Committee of the Heart Committee of the New York Tuberculosis and Health Association.

‡Personal communication forming a memorandum for use by the Committee on Cardiac Clinics of the Heart Committee of the New York Tuberculosis and Health Association.

quently subject to acute inflammation than any other organ of the body, and that those who escape one or more attacks of sore throat may be regarded as exceptions. He concludes from an extensive pathological study that the disease is pyogenic rather than rheumatic in origin, the ulcers at the base of the crypts being the portal of entry of organisms. Similarly, Groedel[5] believes that this affection is a local condition permitting the entrance of certain streptococci and that rheumatism follows only where there is a predisposition to the disease.

That tonsils are not the only possible portal of entry for infection from the mouth is evident when one considers the lymphoid structures constituting Waldeyer's tonsillar ring. Complete tonsillectomy and adenoidectomy cannot remove all this lymphoid tissue. Following operation there is, furthermore, frequently hyperplasia of numerous lymphoid follicles in the nasopharynx and tonsillar fossa. Tonsillectomy is, nevertheless, a therapeutic measure which is widely recommended for the prevention of rheumatic infection in children.

REVIEW OF THE LITERATURE

A review of the literature on the value of tonsillectomy in the prevention of the occurrence and recurrence of manifestations of the rheumatic syndrome is inconclusive. As Cohn[6] has pointed out, the period of observation has frequently been too short and the cases have not been reported in sufficient detail to follow the course of the disease in each individual.

A brief review of the literature may best be undertaken, perhaps, by reproducing Cohn's[6] table, with the addition of experiences reported since its publication (Table I). The number of treated cases reported on in sufficient detail to be included in this table is 1,232. Of these, recurrences of manifestations of rheumatic infection were noted in 43.1 per cent, and no recurrences in 56.7 per cent. Opinions differ among the observers concerning the results of the operation on the recurrence of rheumatic fever.

Period of Observation.—In few instances only did the average length of time of observation after the operation exceed three or four years. A summary of cases reported in the literature about which adequate details were published to make possible tabulation indicates that recurrences became more frequent as the period of observation was extended (Table II).

Age at Operation.—It is to be noted that the age at which the enucleation of tonsils was performed was not considered by any of the observers whose reports are reviewed in Table I. In only 222 instances was the age at operation together with the ages at which subsequent manifestations of infection appeared given in the publications. Tabulation of these data reveals that as the age at which the tonsils

TABLE I[6]

TONSILLECTOMY: ITS EFFECT ON THE OCCURRENCE OF RHEUMATIC MANIFESTATIONS

DATE	AUTHOR	NO. CASES TOTAL	WITH TONSILLECTOMY NO.	PER CENT	NO RECURRENCE NO.	PER CENT	WITH RECURRENCE NO.	PER CENT	WITHOUT TONSILLECTOMY NO.	PER CENT	NO DEVELOPMENT OF MANIFESTATIONS NO.	PER CENT	WITH DEVELOPMENT OF MANIFESTATIONS NO.	PER CENT	REMARKS
Complete Tonsillectomy															
1908	Rosenheim		10		10	100.0	0	0							
1911	Archibald	7	7		5	71.4	2	26.8							
1915	Young	21	21		6	28.6	15	71.4							
1917	Crowe, Watkins and Rothholz	49	49		28	56.3	21	43.7							
1920	St. Lawrence	85	85		54	63.5	31	36.5							
1923	Hunt and Osman	144	66		31	47.0	35	53.0	78		45	58.0	33	42.0	All cases
		(99)	(50)				(23)	(46)	(46)				(15)	(33)	After first attack
		(48)	(16)				(12)	(75)	(32)				(18)	(56)	After later attacks
1924	Ingerman and Wilson	167	70		17	24.0	53	76.0	97		19	19.6	78	80.4	
1924	Dulaney		22		22	100.0	0	0							
1926	R. Miller	133	45		18	40.0	27	60.0	(83)						
1926	R. Miller (A. P. Thompson)	16	6		6		10	62.5							
1926	Mackie	299	80		46	57.5	34	42.5	207		82	39.7	125	60.3	After first attack
			12		0	0									Before first attack
1927	Robey and Freedman[7]	454	169		122	72.1	47	27.9	212		160	75.5	52	24.5	
1927	Kaiser[8]	525	525		316	60.0	209*	39.8							Rheumatism
		102	65		18	27.7	47†	72.1							Chorea
Totals			1232		699	56.7	531	43.1	594		306	51.5	288	48.5	Rheumatism
Partial Tonsillectomy															
1921	St. Lawrence	9	9		1	11.2	8	88.8							
1924	Ingerman and Wilson	18	18		4	22.3	14	77.7							
1927	Robey and Freedman	32	32		17	53.2	15	46.8							
Totals		59	59		22	37.3	37	62.7							

*93 occurred for the first time after operation.
†32 occurred for the first time after operation.

TABLE II*

TONSILLECTOMY

RECURRENCE OF RHEUMATIC FEVER AND CHOREA AND THE DURATION OF OBSERVATION

MANIFESTATION	DURATION OF OBSERVATION AFTER TONSILLECTOMY YEARS	CASES EXHIBITING MANIFESTATIONS BEFORE TONSILLECTOMY		AFTER TONSILLECTOMY					
				RECURRENCE				NO RECURRENCE	
				SAME MANIFESTATION		OTHER MANIFESTATION			
		NO.	%	NO.	%	NO.	%	NO.	%
Rheumatic fever	1 or less	16	100	2	12.5	3	18.7	11	68.7
	1 to 3	61	100	9	14.7	17	27.9	35	57.4
	More than 3	41	100	16	24.4	10	24.4	21	51.2
	No report	5	—	2	—	0	—	3	—
Chorea	1 or less	7	100	1	14.3	2	28.6	4	57.1
	1 to 3	51	100	17	33.3	8	15.7	26	51.0
	More than 3	26	100	12	46.2	1	3.8	13	50.0
	No report	9	—	8	—	0	—	1	—

*Table compiled from reports of Young,[9] Crowe, Watkins and Rothholz,[10] St. Lawrence,[11] and Ingerman and Wilson.[12]

TABLE III*

TONSILLECTOMY
RELATION OF SUBSEQUENT MANIFESTATION TO AGE

AGE AT OPERATION YEARS	TOTAL		RECURRENCE		NO RECURRENCE	
	NO.	%	NO.	%	NO.	%
0-5	28	100	17	61.	11	39.
6-9	88	100	49	56.	39	44.
10 and over	106	100	53	50.	53	50.
TOTAL	222	100	119	54.	103	46.

*Table includes data reported by Crowe, Watkins and Rothholz,[10] St. Lawrence,[11] and Ingerman and Wilson.[12]

were enucleated increased, the proportion of cases that recurred to those that did not recur decreased (Table III).

Controls.—In only four* of the series reported were corresponding untreated groups studied as controls, and in only two† did the treated children show a lesser incidence of recurrence than the untreated. Even in these two series, however, as many as 80.4 per cent and 60.3 per cent of the untreated children suffered at least one return of the rheumatic condition. It is to be regretted that Kaiser,[8] although he gives the incidence rate of the various rheumatic manifestations upon the treated and untreated children, does not specify whether the incidence of infection among the latter occurred during a period comparable in duration with that which elapsed in the treated cases after the time of operation. As was pointed out in an editorial in a recent issue of *The Lancet*, there is no justification for his statement that "It is fair to conclude that the tonsils undoubtedly are a focus in many cases of rheumatic fever. Their removal offers considerable protection against recurrent attacks, and when the tonsils are removed before symptoms have developed, the chances for escaping rheumatic infection are appreciably increased."

Obviously, when opinions cover so wide a range as those which we have repeated, knowledge concerning this matter is still imperfect. The literature of this subject is large, but contains, we think after reviewing it, few descriptions of the disease or of cases that lend themselves to critical analysis. It has seemed to us to be more important to report the results of our studies than to review data which are either incomplete or are collected from points of view which are preconceived.

INFLUENCE OF TONSILLECTOMY ON THE COURSE OF THE RHEUMATIC INFECTION IN CHILDREN

In this investigation we have made use of the records of 413 rheumatic children reported in a previous paper.[15] These children were observed over a period ranging from one to ten years. In 247 cases

*Hunt and Osman,[6] Ingerman and Wilson,[12] Mackie,[14] Robey and Freedman.[7]
†Ingerman and Wilson[12] and Mackie.[14]

the tonsils were removed. The remaining 166 served as controls. We have attempted to present the data in detail* and to analyze the results, bearing in mind the age of the child at the time of operation, the age at the onset of the infection, and the period of observation after operation. There are included as recurrences of manifestations of infection (evidence of activity) polyarthritis, growing and joint pains, chorea, nodules, and carditis. Tonsillitis was not included, for reasons stated in a previous paper[15] and therefore will be considered separately.

Recurrence of Infection After Tonsillectomy.—Of 245† children subjected to tonsillectomy, manifestations of rheumatic infection recurred in 117, or 47.7 per cent; infection appeared for the first time in 85, or 34.7 per cent; that is to say, there was a total incidence of rheumatic infection subsequent to tonsillectomy in 202 cases, or 82.4 per cent of all children operated upon. In only 43 cases, or 17.5 per cent, therefore, was there no manifestation of rheumatism after the operation (Table IV).

TABLE IV

TONSILLECTOMY

RELATION OF SUBSEQUENT MANIFESTATION TO AGE

AGE AT OPERATION YEARS	% OF TOTAL	TOTAL		AFTER TONSILLECTOMY					
				RECURRENCES		FIRST INFECTION		NO RECURRENCE	
		NO.	%	NO.	%	NO.	%	NO.	%
0-5	22.8	56	100	17	30.4	35	62.5	4	7.1
6-9	47.4	116	100	59	50.9	41	35.3	16	13.8
10 and over	29.8	73	100	41	56.2	9	12.2	23	31.5
Total	100.0	245	100	117	47.7	85	34.7	43	17.5

TABLE V

TONSILLECTOMY

RELATION OF SUBSEQUENT MANIFESTATION TO AGE

AGE AT OPERATION YEARS	TOTAL		AFTER TONSILLECTOMY					
			RECURRENCES		FIRST INFECTION		NO RECURRENCE	
	NO.	%	NO.	%	NO.	%	NO.	%
0-5	56	22.8	17	14.5	35	41.1	4	9.3
6-9	116	47.4	59	50.5	41	48.3	16	37.2
10 and over	73	29.8	41	35.0	9	10.6	23	53.5
Total	245	100.0	117	100.0	85	100.0	43	100.0

Age at Operation and Recurrent Infection.—In 116 patients, or 47.4 per cent, almost one-half, the operation was performed at ages between six and nine years (Table IV). It is important to note that this is also the age at which the greatest number of children became in-

*The age at tonsillectomy, age at onset of infection, and at recurrences of various manifestations of infection have been charted for each child in Fig. 6 in a previous paper.[15]

†Two cases were omitted in the tabulations because of incomplete data.

fected. It is important to note, also, that of children infected after operation, tonsillectomy was performed between the ages of six and nine in approximately 50 per cent of the cases. (Table V.) Of the treated children who did not experience subsequent infection, however, the operation was performed in half of the cases after the age of ten years was reached. As was indicated in the previous paper, there appears to be a diminution in susceptibility to rheumatic infection beginning at about the age of ten. It seems probable, therefore, that the age at which the operation was performed, and not the operation itself may be the significant factor in the incidence of nonrecurrence.

This point is further emphasized when we consider the relative incidence of recurrence and nonrecurrence in groups of children oper-

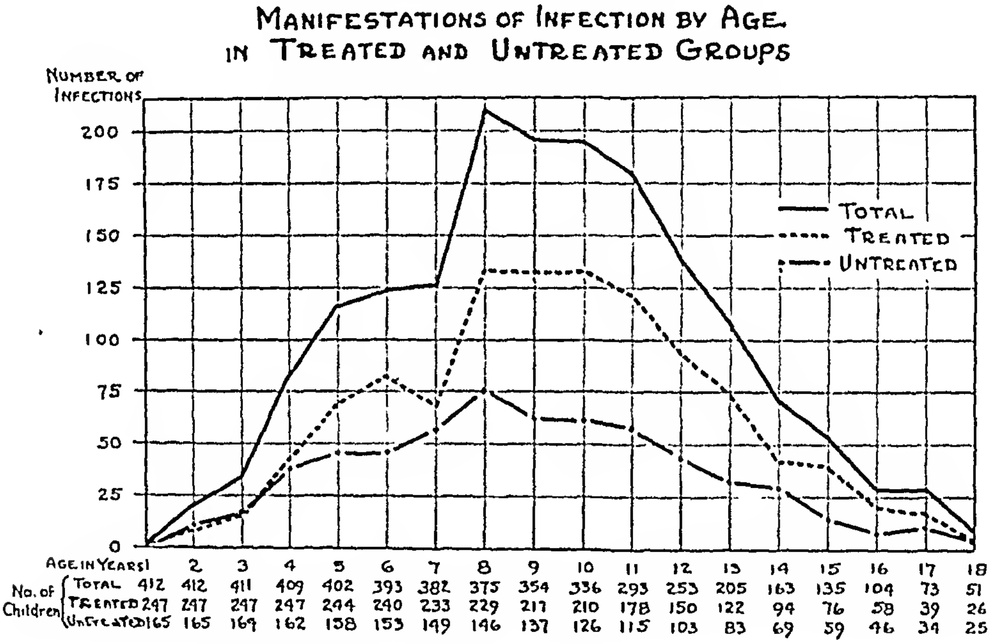

Fig. 1.

ated on at different ages. When the age is less than five years, 7.1 per cent experienced no recurrence; of those operated upon between the ages of six and nine, 13.8 per cent did not recur, and at age ten or over, 31.5 per cent were not followed by recurrences (Table IV). In other words, as the age at operation increases, the likelihood of recurrence diminishes.

Incidence of Recurrent Infection in Treated and Untreated Groups.—As was previously pointed out, beginning at two years, the incidence of manifestations of infection increases with each succeeding age, reaches a peak at the age of eight, and then gradually but progressively declines. This was found to be true in both treated and untreated children. In general, the trend of the curves is the same for both groups (Fig. 1).

From our experience in the observation of 245 treated and 165* untreated children, we have attempted to learn what the likelihood is of recurrence at each age for children in both groups (Fig. 2). The ordinates (Curves A and B) show the average number of manifestations of infection which a child has experienced before a given age. In Curve A, this is the number before operation. In similar fashion Curves C and D show the average number of infections experienced after each age. In the case of Curve C it is the average number of infections experienced after operation. The curves lead us to expect, for instance, that a child that presents itself for operation at the age of six years will have suffered, on the average, one attack of infection, but that after operation it will yet experience more than three, probably four, attacks. A child of like age not operated upon, while

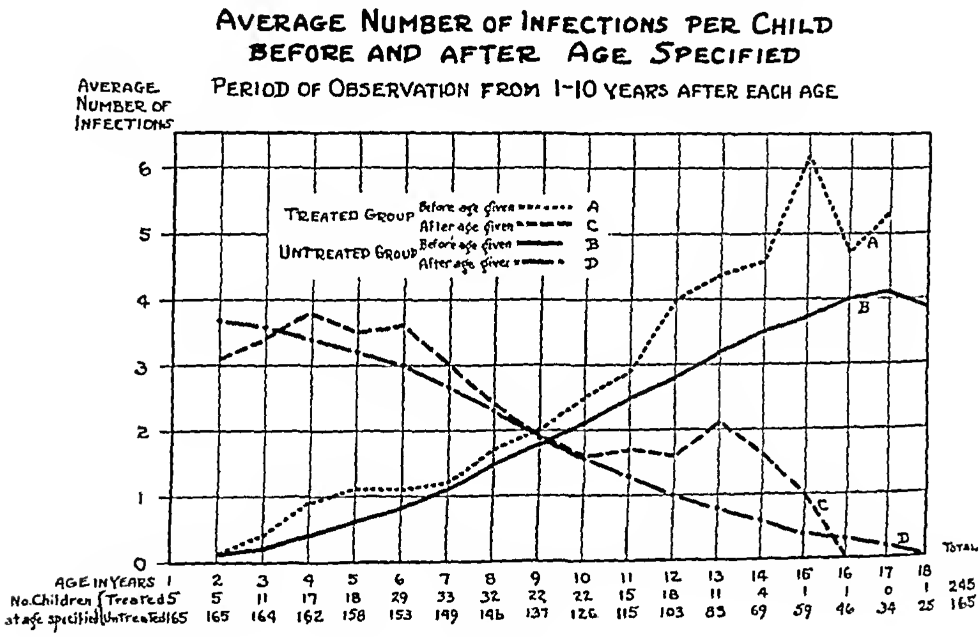

Fig. 2.

it will have experienced a somewhat lesser number of infections, will likewise experience about three times as many attacks in subsequent years. Similarly, a child that presents itself for operation at the age of thirteen years will have suffered, on the average, four attacks and is likely to exhibit after operation two more attacks. A child of like age not operated upon is likely to experience but one subsequent attack.

In general, these curves seem to express the following:

1. As the age increases, the average number of attacks of infection a child may anticipate decreases. At nine years, the average child will have suffered (Curves A and B) as many attacks as it will experience in subsequent years (Curves C and D).

*One case was omitted in the tabulation because of incomplete data.

2. This is true whether a child has or has not been operated upon. The curves for the two groups are almost parallel. In both groups the incidence of infection increases with age (Curves A and B).

3. Although the curves for the two groups are approximately parallel, those representing the untreated children are at almost every point lower than those representing the treated group. That is to say, at each age the untreated children experienced fewer infections than did those that were treated. One may assume from these figures that the untreated children were less susceptible to recurrent attacks of infection and that, perhaps, for this reason they were not subjected to tonsillectomy—a therapeutic measure often applied, especially to cases of severe and recurrent infection, in the absence of knowledge of more certain therapy. On the basis of this assumption, the untreated children in this series do not constitute a perfect control group.

4. Excision of the tonsils seems to have no effect on the recurrence of rheumatic infection.

If this analysis of our data is correct, it may be an explanation of the contradictory results obtained by various observers concerning the effect of tonsillectomy in rheumatic children. If the majority of the children reported on in any series have reached an age of ten years or more at the time of operation, the results of the operation might appear to be favorable as judged by recurrent infection. If, on the other hand, the sample is overloaded with cases that were operated on at earlier ages, a high incidence of recurrence would be the probable result and the benefit of tonsillectomy would very likely be questioned.

Period of Observation.—A study of the literature reveals the fact that the percentage of recurrences in treated children increases with time (Table II). We have attempted to consider this factor by drawing curves similar to those already presented, limiting our data in each case to children who were observed for varying numbers of years after each age (Fig. 3). In general, the curves are in agreement with our first series. At every age subsequent to an age ranging from seven to nine years, a child, on the average, experienced fewer attacks of infection than it had before the age specified.

It is apparent from these curves, also, that the longer the period of observation, the greater is the average number of infections at each susceptible age. This is true in the treated as well as in the untreated groups. After the age of nine years, when, as we have shown, susceptibility to infection appears to be lessened, prolonged periods of observation have no effect on the number of recurrences.

Tonsillitis.—Of the 247 children from whom the tonsils were removed, 124, or 50.2 per cent, experienced recurrent tonsillitis, and 123, or

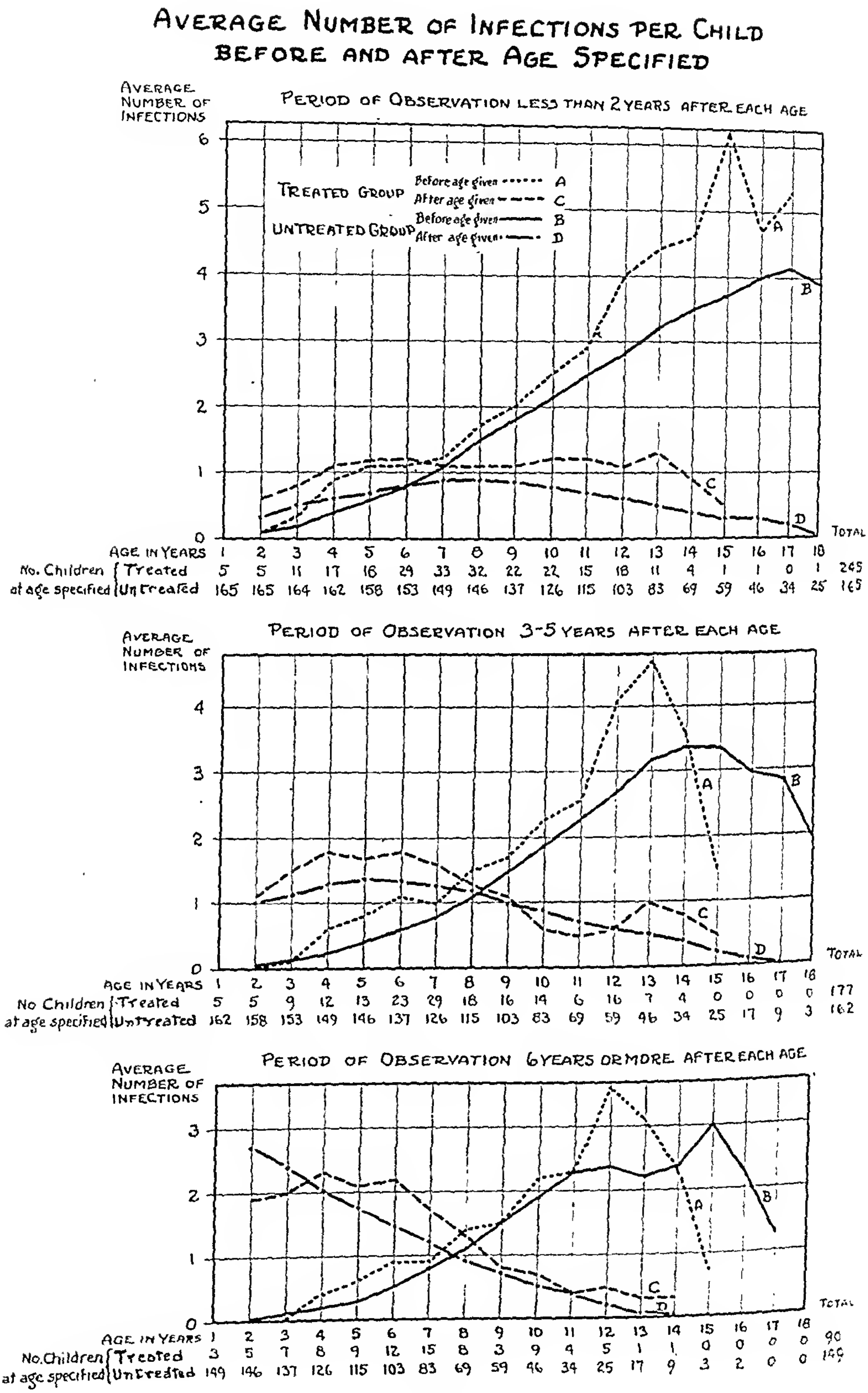
AVERAGE NUMBER OF INFECTIONS PER CHILD
BEFORE AND AFTER AGE SPECIFIED
AVERAGE NUMBER OF INFECTIONS
PERIOD OF OBSERVATION LESS THAN 2 YEARS AFTER EACH AGE
TREATED GROUP Before age given A
After age given C
UNTREATED GROUP Before age given B
After age given D
A
B
C
D
TOTAL
AGE IN YEARS 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
No. Children at age specified Treated 5 5 11 17 16 29 33 32 22 22 15 18 11 4 1 1 0 1 245
Untreated 165 165 164 162 158 153 149 146 137 126 115 103 83 69 59 46 34 25 165
AVERAGE NUMBER OF INFECTIONS
PERIOD OF OBSERVATION 3-5 YEARS AFTER EACH AGE
A
B
C
D
TOTAL
AGE IN YEARS 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
No Children at age specified Treated 5 5 9 12 13 23 29 18 16 14 6 16 7 4 0 0 0 0 177
Untreated 162 158 153 149 146 137 126 115 103 83 69 59 46 34 25 17 9 3 162
AVERAGE NUMBER OF INFECTIONS
PERIOD OF OBSERVATION 6 YEARS OR MORE AFTER EACH AGE
A
B
C
D
TOTAL
AGE IN YEARS 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
No. Children at age specified Treated 3 5 7 8 9 12 15 8 3 9 4 5 1 1 0 0 0 0 90
Untreated 149 146 137 126 115 103 83 69 59 46 34 25 17 9 3 2 0 0 149

Fig. 3.

TABLE VI

TONSILLECTOMY

INCIDENCE OF TONSILLITIS IN TREATED AND UNTREATED CHILDREN

	TOTAL		TONSILLITIS		NO TONSILLITIS	
	NO.	%	NO.	%	NO.	%
Treated	247	100	124	50.2	123	49.8
Complete enucleation	(220)	100	(107)	(48.6)	(113)	(51.4)
Incomplete enucleation	(27)	100	(17)	(63.0)	(10)	(37.0)
Untreated	166	100	80	48.2	86	51.8
Total	413	100	204	49.4	209	50.6

49.8 per cent, did not (Table VI). Of 166 children who were not operated upon, 80, or 48.2 per cent, gave a history of recurrent tonsillitis, and 86, or 51.8 per cent, did not. The influence of tonsillectomy on the recurrence of tonsillitis and sore throat showed on analysis 124 case records, 50, or 40.3 per cent, in whom there was recurrence and 74, or 59.7 per cent, in whom there was none. In 107, or 86.3 per cent, enucleation was complete and in 17, or 13.7 per cent, it was incomplete.

The possible importance of complete and incomplete tonsillectomy has been stressed by some observers. In this series tonsillar tissue was left in 27 who were reexamined after tonsillectomy. A comparison of the average number of infections experienced by these children after tonsillectomy showed no difference from those whose tonsils had been completely enucleated.

COMMENT

When the etiological agent, the portal of entrance, and the focus of infection are unknown in a disease, it is difficult to estimate the influence of any one therapeutic measure. This is particularly true of tonsillectomy in its relation to the prevention of rheumatic infection in children.

A summary of the available data on the value of tonsillectomy in this disease is inconclusive for reasons already discussed. It is obvious that before we can expect to obtain results based on conclusive evidence, it is necessary that:

1. The number of cases studied be greatly increased.
2. Criteria for rheumatic infection and disease of the tonsils be uniform.
3. Enucleation of the tonsils be complete and other possible foci of infection be excluded.
4. Cases be so recorded that it may be possible to deduce what has actually been the course of events.
5. The duration of observation be extended.
6. Cases not operated upon be studied as control groups; that such groups be comparable, so far as is possible, to the treated cases, in

respect to age, constitution, duration of observation, virulence of infection, and susceptibility to its recurrence.

This investigation includes a small series of 247 children from whom the tonsils were removed. The results as judged by the occurrence and recurrence of manifestations of infection after operation do not indicate that tonsillectomy is to be advised as a routine therapeutic measure for the prevention of rheumatic heart disease in children. One may urge that this particular series of children was unusually susceptible, that the etiological agent was particularly virulent, or that other foci were still present. The question of incomplete tonsillectomy cannot be discussed from our limited data. Its importance has, we believe, been overemphasized. The impossibility of complete surgical removal of all possible foci in the nasopharynx is obvious. To expect tonsillectomy to prevent the occurrence of rheumatic heart disease does not seem justified in the light of present insufficient knowledge of this disease.

SUMMARY

1. Of 413 rheumatic children observed over a period of from one to ten years, 247 were subjected to tonsillectomy.

2. Manifestations of infection recurred in 47.7 per cent and appeared for the first time in 34.7 per cent of the treated children.

3. In only 17.5 per cent was there no manifestation of rheumatism after the operation.

4. In rheumatic children less than nine or ten years of age, recurrent attacks were frequent, whether or not tonsillectomy had been performed. In older children recurrent attacks became less frequent regardless of enucleation of tonsils.

5. The age at which tonsillectomy was performed and not the fact of tonsillectomy appeared to be the significant factor in the incidence of nonrecurrence of infection after operation.

CONCLUSION

The routine removal of tonsils for the prevention of rheumatic heart disease in children is not based on conclusive data.

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ON THE LYMPH FLOW OF THE HUMAN HEART, WITH REFERENCE TO THE DEVELOPMENT OF THE CHANNELS AND THE FIRST APPEARANCE, DISTRIBUTION, AND PHYSIOLOGY OF THEIR VALVES*

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IN MY researches on the genesis, arrangement and action of the valves in the lymphatic system,† I discovered some notable features respecting their initial appearance and distribution in diverse parts of the human body.‡ In an organ like the lung, for instance, which does not exercise its function until the close of fetal life, the valves arise synchronously with those of the systemic lymphatics—only the ones in the neck and mediastinum appearing earlier. But in the several areas of the lung remarkable differences obtain in the number of valves laid down. In the fetus and newborn they occur abundantly in the pulmonary pleura facing the heart and are somewhat less numerous in that facing the diaphragm and the anterior thoracic wall, but they are absent or at best very scarce at the apex and in the vertebral and the dorsal and lateral costal surfaces of the lung. This strikingly unequal disposal of the lymphatic valves suggests but one explanation, namely, that the excursions of the beating heart, for example, impinging on the medial side of the lung and tending to interfere with the steady flow of lymph during its respiratory expansion, led to the evolution of such regulators whereby the direction of the current is maintained and safeguarded. I believe that this particular illustration of the arrangement of the lymphatic valves represents the most lucid demonstration yet observed of their fundamental purpose.

Such morphological peculiarities as these, and speculations on their physiological significance, induced me to seek information concerning the genetic, as well as functional, history of the lymphatic valves in the heart, especially because this organ is the first permanent one to assume its definite duties in the life of the individual.

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†In 1923, the directors of the Bache Fund of the National Academy of Science made a grant of one hundred dollars, and the committee on grants of the American Association for the Advancement of Science set aside the same sum to aid me in my investigations on the evolution and comparative morphology of the lymphatic system. Since considerable time will still elapse before a comprehensive monograph, which is being prepared, is ready for publication, I take the opportunity here and in other papers dealing with the subject of acknowledging the assistance given in pursuance of that plan.

‡The Genetic History of the Valves in the Lymphatic System of Man. Am. Jour. Anat., 1928, xl, 413.

Further Observation on the Numerical Variability, Position, Function, and Fate of the Valves in the Human Thoracic Duct, Anat. Rec., 1928, xxxviii.

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Three hundred years have elapsed since the rediscovery of the lymphatics by Asselli (1622), and though a goodly array of papers has dealt directly or indirectly with these vessels of the heart, much obscurity still prevails about them. Their origin and differentiation in the human heart, not to mention that of their valves, has never been examined, and regarding their rôle in its activities "physiology is silent," as one author succinctly remarks.

The growth of the knowledge we have of the lymph channels of the heart has been halting. Mascagni, in his famous treatise on the lymphatic system printed in 1784, cites Rudbeck, Nuck, and Cassebohm as having seen them earlier. Cruikshank, whose work was published two years after Mascagni's also confirmed their findings, but all of these investigators had only perceived the superficial lymphatics. Later these pericardial vessels were studied in man and other mammals by Gurlt (1844), Leyh (1859), Teichmann (1861), Eberth and Belajeff (1866), Wedl (1872), Bizzozero and Salvioli (1787), Sappey (1885), Tanasescu (1907), Rainer (1909), and others, so that today we possess an adequate picture of their course and topography. Most of the investigators named also traced the path of the lymph stream from the heart to the nodes of the mediastinal territory. Most recently (1928), Shore has undertaken an inquiry into this phase of the subject from the standpoint of infections.

It is when we turn to the matter of deep cardiac lymphatics that we meet with radical differences of opinion regarding their existence and nature. Leyh (1859), it seems, was the first to point out their presence in the myocardium, and Luschka (1863) described them as forming a rich network discharging into the peripheral plexus at the furrows and apex of the heart. However, Eberth and Belajeff (1866) claimed that the heart muscle was deficient in such vessels. Henle (1868) and Schweigger-Seidel (1871) likened the organ to a "lymphatic sponge," they assuming that all the interstices between and around the fasciculi contained and conveyed lymph. By means of the "Einstich-methode," or injection by puncture, Skwartzoff (1874), Skworzow (1874), and Navalichin (1882) filled a myocardial net of channels which they interpreted as lymphatic, and which they said was lined throughout with endothelium. Salvioli (1878), supported by Masini (1887), could not discern continuity between the lymph vessels of the interfascicular septa and the intermuscular spaces, and hence rejected the simile of the "lymphatic sponge" as applied to the cardiac musculature. On the other hand, Bianchi (1886) was led by experiments to believe that no true lymphatics—that is, vessels possessed of an intima—occur in the myocardium, and that the lymphatic fluid percolates through its ill-defined crevices, eventually to be absorbed by the pericardial channels. A year later, Albrecht (1887), by injecting the living mammalian heart and letting its natu-

ral movements disseminate the injected mass, reached the conclusion that a widespread and endothelial-lined lymph capillary plexus pervaded its muscle. But Ranvier (1889) again revived the idea of the "lymphatic sponge."

In an attempt to settle the controversy, Nyström (1897) employed three methods: those of injection, sectioning, and Golgi impregnation, on fresh hearts of the dog, cat, pig, calf, sheep, rabbit, and man. His inference was that the lymphatic pathways of the heart muscle are composed of a combination of interstitial spaces and true endothelial-lined vessels. The spaces themselves are of complicated form and are in intimate relation to the muscular elements, in so far as they not only surround the individual fibers but also send minute radial extensions into their sarcoplasm. Notwithstanding all the evidence to the contrary, Poirier and Cunéo (1902) returned to Sappey's (1885) earlier attitude of denying altogether the existence of definite lymphatics throughout the myocardium.

The most elaborate and, in my judgment, the most decisive work yet done to demonstrate the actual occurrence and character of myocardial lymphatics was carried out by Bock (1905). Confronted squarely by the pertinent criticism, already recognized by his immediate predecessors, that the results derived from blindly injecting the myocardium by puncture do not permit absolute distinction between lymphatic and hemal plexuses, he made use of the method of double injection. After flushing the blood from the coronary vessels and filling them with carmine gelatine under pressure, and then forcibly injecting Berlin blue into the myocardium, he was able to reveal two complex yet entirely separate vascular networks both possessing distinct walls. He plainly asserts that diffusion of the injecta from one set of vessels into the other was not visible. Nevertheless, Cash (1917), on the basis of a study of the formation of the lymphatics in the heart of the embryo and fetal pig, not only maintained that the myocardial plexus of lymph channels is not as extensive as Bock believed—they becoming fewer and smaller the deeper they penetrate toward the endocardium—but he intimated that Bock did confuse those vessels.

Nor is there unanimity of opinion concerning the existence of lymphatics in the endocardium. Contrary to Eberth and Belajeff (1866) and Wedl (1872) who had reported a plexus of these canals which enter even into the flaps of the mitral and tricuspid valves, Schwartz-Skwartzoff (1872) said he was unable to find them. But Sappey's (1885) injections with mercury did disclose such a network, an observation that was corroborated by Nyström (1897) who also agreed that it flourished better in the ventricles than in the atria. Yet Cash (1917) contends that "claims for an endocardial lymphatic plexus are evidently founded on partial injections of the His bundle." Although I

cannot deny the reality of lymph vessels in the inner lining of the heart, the objection of Cash is warranted. Before the existence of the atrioventricular bundle was known, the channels manifested by injections into it naturally were assigned to the lymphatic system. Indeed, further research has still to prove that the injectable sheaths which follow the intricate ramifications of that conduction bundle are not in direct communication with the true lymphatics.

For the sake of clarity in the account of the arrangement of the lymphatic valves, the following image of the lymph drainage in the

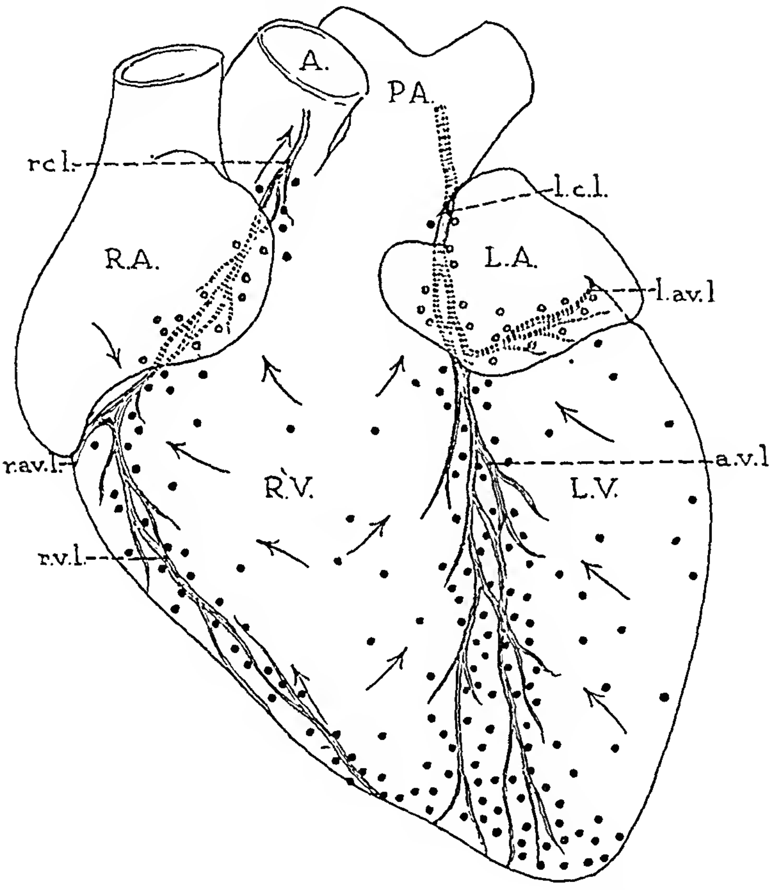

Fig. 1.—Diagram of the anterior surface of the fetal heart, from the middle of intrauterine life, showing the course of the chief channels of the pericardial lymphatic plexus, and the distribution of its values. Approximately 4 X. *R.V.*, *L.V.*, *R.A.*, and *L.A.*, right and left ventricles and atria, respectively; *A*, ascending aorta; *P.A.*, trunk of pulmonary artery; *a.v.l.*, anterior ventricular lymphatic; *r.v.l.*, right ventricular lymphatic; *r.av.l.* and *l.av.l.*, right and left atrioventricular lymphatics; *r.c.l.* and *l.c.l.*, right and left cardiac lymphatics, the efferent lymph ducts of the heart; (It should be stated that these lymphatics are portrayed schematically, no attempt being made to show the great irregularity of caliber and the plexiform character, so characteristic of even the larger lymphatics). The arrows indicate the course of the lymph stream as determined from the directions in which the valves point. The location of the valves, marked by dots, was plotted in a graphic reconstruction.

human heart may be constructed in its main outlines. From the delicate radicles and meshes of a more or less extensive net of vessels spread throughout the endocardium and myocardium, the lymph is collected by the interfascial channels which, closely paralleling the myocardial tributaries of the coronary blood vessels, transport it to

the external layer of the heart. Here, particularly along the furrows, they emerge as relatively large channels the frequency of which, as seen in serial sections of the fetal heart, dispels any remaining doubt about the existence of kindred channels in its depth. The pericardial lymphatic plexus itself, which receives these deep vessels and which is so clearly portrayed in the figures of Sappey and Tanasescu, for example, covers the ventricular district of the heart lavishly, the atrial scantily. In my own diagrams (Figs. 1 and 2) merely the course of the major collecting conduits of this superficial plexus is pictured.

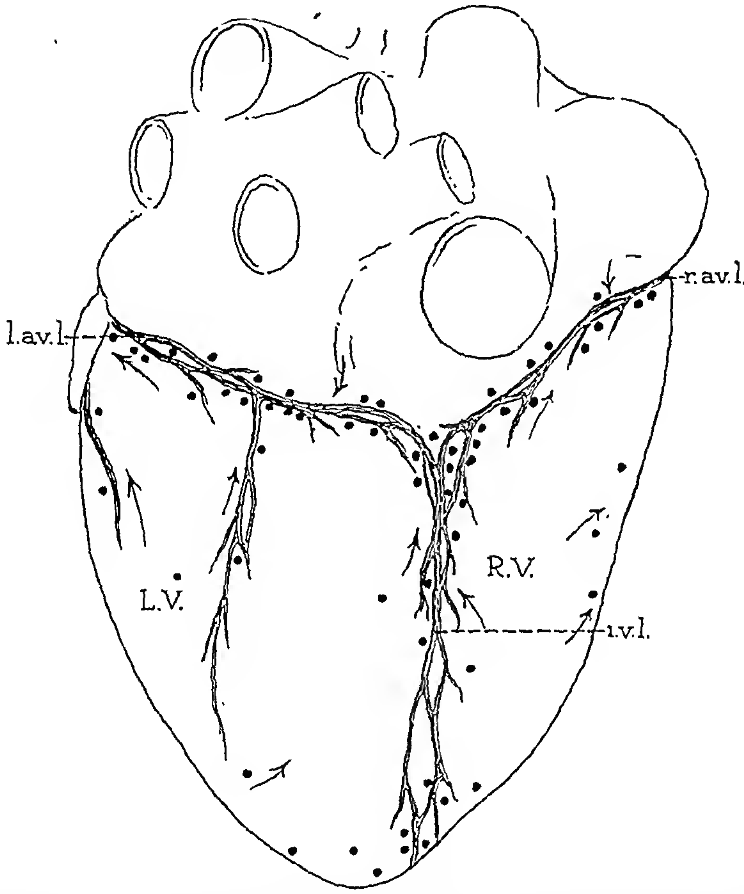

Fig. 2.—Diagram of the inferior or diaphragmatic surface of the heart illustrated in Fig. 1. *i.v.l.*, inferior ventricular lymphatic. Other references as in Fig. 1.

Of these conduits—plexiform and twining about the contiguous coronary arteries and veins—the one (a.v.l., Fig. 1), situated in the anterior ventricular sulcus and draining the greater part of the front of the heart except at the right, unites with the left atrioventricular lymphatic (l.av.l.), running from the diaphragmatic surface, to form the left trunk of the two principal lymphatic outlets of the heart. The efferent (l.e.l.) so formed proceeds upward between the left atrium and the pulmonary arterial trunk, and then bending to the posterior side of the latter traverses in some cases an intrapericardial and retropulmonary lymph node, more rarely a subaortic one, on its way to

the tracheobronchial group of nodes. Similarly a ventricular lymphatic (r.v.l.) drains much of the right ventricle, is joined by an atrioventricular lymphatic (r.av.l.) coming from the rear, and is continued as the right principal lymphatic outlet (r.c.l.) of the heart. This channel passes along the forward side of the ascending aorta to enter an anterior mediastinal node, which in the infant is retrothymic and in the adult is situated at the root of the left common

Fig. 3.—Photomicrograph of part of a transverse section through a 30 mm. (2.2 months) human fetus at the level of the base of the heart. X 27. *r.c.l.* and *l.c.l.*, right and left cardiac lymphatics, representing the primary lymph channels invading the heart during development, and retained throughout life as the efferent ones. *t.d.*, thoracic duct; *t.l.*, pretracheal lymphatic plexus; *R.A.* and *L.A.*, right and left atria; *A*, ascending aorta; *P.A.*, trunk of pulmonary artery; *S.V.C.*, superior vena cava; *b.*, bronchi; *oe*, esophagus; *a*, descending aorta.

carotid. In few instances the right trunk on leaving the heart bears a small intrapericardial node, preaortic in position (Tanasescu). It is evident that variations occur; for example, the right trunk may occasionally (3 per cent) go behind the pulmonary artery to combine with the left trunk.

Since the literature is mute on the development of the lymphatics in the human heart, it was necessary to determine the first appearance and situation of these before considering that of their valves. In an embryo of 30 mm.—at the end of the second lunar month of pregnancy—two plexiform extensions from the mediastinal lymphatics have entered the base of the heart. One, arising as a branch from the upper reaches of the thoracic duct, near the junction of this duct with the left jugular lymph sac, and extending down in front of the left carotid and to the left of the aortic arch, comes to lie (r.c.l., Fig. 3) in the groove between the pulmonary artery and the ascending *aorta*. It then grows out ventral to this vessel and along the right coronary artery, although in the 30 mm. specimen it had made little progress here, its tip soon vanishing in the mesenchyma. The other extension (l.c.l.), the more important of the two and a derivative of the pretracheal lymphatic plexus, runs dorsal to the pulmonary artery and then to its left, subsequently to be prolonged along the left coronary artery. The pretracheal plexus itself largely represents a downward growth from the right jugular lymph sac by the side of the right cardinal vein, though it is also in anastomotic connection with projections from the thoracic duct.

The two original or primary lymphatic extensions into the embryonic heart are retained as the efferent lymph passages of the adult organ. Though there is nothing to prevent the cardiac lymph stream from taking its way to the lymphaticovenous gateways at either the right or the left jugulosubclavian regions, it seems the pathway to the right via the tracheal plexus and the right bronchomediastinal trunk assumes greater significance.

In the 40 mm. human embryo the primary lymphatics of the heart have extended far along the coronary arteries in the interventricular and atrioventricular sulci. Because of the limited human embryonic material available, I was unable to ascertain how the formation and elongation of the earliest cardiac lymphatics are achieved, whether by centrifugal sprouting or by the centripetal coalescence and addition of discrete lymphatic spaces, as happens in the genesis of the main systemic conduits. It may be pointed out, however, that the mesenchymal tissue in the furrows is wider and of looser texture than elsewhere in the visceral pericardium.

During the third month of intrauterine life a net of lymph vessels expands rapidly over the periphery of the heart so that by the beginning of the fourth month the greater part of the surface is furnished with them. Ultimately this pericardial plexus becomes intricate and close-meshed over the ventricular territory, but always remains more restricted and simple over the auricular.

In his study of the development of the cardiac lymphatics in the pig, Cash noticed that the superficial plexus is established almost com-

pletely before the invasion of the myocardium commences. His endeavor to inject the myocardial lymphatics in specimens ranging from 60 to 150 mm. in length failed to reveal many such vessels. Indeed, he implies the conclusion already touched upon that neither are they as abundant in the myocardium as Bock supposed nor do they appear in the endocardium—a view which I am not prone to accept.

At the end of the third or the beginning of the fourth month of prenatal life, the first valves have their inception in the developing pericardial lymphatic plexus. The earliest ones arise in the main channels accompanying the coronary blood vessels. Shortly after, during the multiplication of connections in the network and its differentiation, in which the abandonment and collapse of some channels and the increment of others is dominant because of the shifting hydrostatic conditions ensuing from the active development and growth of the heart as from that of any other organ, valves spring up also in the more distant parts of the plexus.

Despite the early demands put on the heart in the formation of the individual, its finished state is accomplished no earlier, it seems, than that of most other organs. Certainly this holds true as regards the acquisition of its lymphatics and their valves, in which process it does not even surpass the lungs. To say that during ontogenesis the details of organization are engendered in conformity with some determinate pattern or memory inherent in the protoplasm is to mask our ignorance; yet it is impressive that such creation occurs irrespective apparently of immediate functional exigency. The cells that build the lymphatic system are capable of proliferating valves between the end of the second and the beginning of the fifth month of fetal life and probably lose that power thereafter. The oldest or earliest lymphatic territory acquires its valves first. I have shown previously* that at approximately two months some have already appeared in the tributaries of the jugular lymph sac in the neck region. As early as three months they are encountered in such a distal area of the body as the femoral trigone, and but a short while after they abound throughout the lymphatic plexus of the entire lower extremity. It is at this time too that they are generated in the heart and lungs.

In their mode of origin and development the valves of the cardiac lymphatics do not differ from those elsewhere in the body. For a detailed description of the genetic procedure the reader is referred to my paper in the *American Journal of Anatomy*.† It suffices to say that, in the large systemic trunks like the thoracic duct, their inception and perfection is identical with that of the venous valves,‡

*Loc. cit., footnote, page 210.

†Loc. cit., footnote page 210.

‡Otto F. Kampmeier and Carroll La Fleur Birch: The Origin and Development of the Venous Valves, With Especial References to the Saphenous District in Man, Am. Jour. Anat., 1927. xxxviii, 451.

whereas in the peripheral plexuses including those of the heart, lungs, etc., it varies according to whether they originate at confluences of vessels already completed, or at confluences just being established. In the one case the valve issues from an endothelial proliferation that encircles the entrance of one channel into another, in the other the valve is produced from the tip or bud of a small vessel that grows at a tangent into the lumen of a bigger vessel. An example of a fully

Fig. 4.—Photomicrograph of a section at the surface of the ventricular portion of the heart in a fetus of 105 mm. (3.8 months). X 270. *P*, pericardium; *M*, outer margin of myocardium; *l*, lymph vessels, with a valve at *; *V*, branch of a coronary vein.

formed valve in the pericardial lymphatic plexus is depicted in longitudinal section in Fig. 4 (at *).

When we look at the distribution of the lymphatic valves in the heart, we find that the larger channels of the pericardial plexus are supplied more liberally with them, as we should expect, than the more terminal meshes. Curiously, too, they are more plentiful on the anterior than on the inferior or diaphragmatic face of the heart. Comparatively, they are most numerous at the apex where the larger

conduits of the network are in direct union. It is true that these observations were made on the fetal organ, but there is evidence to favor the assumption that the production of lymphatic valves is finished before birth and that their relative numerical differences on the several sides of the heart persist. With few exceptions all of the valves were found in the ventricular portion. For example, of the nearly 300 valves counted in the heart of a 105 mm. (3.8 mo.) fetus, not more than four or five occurred on the atrial surface. In the depth of the myocardium they were absent, but near its periphery an occasional one was seen in the mouths of the interfascial lymph channels pointing outward to the pericardial.

In approaching the physiological side of the subject, it is obvious first of all that the direction in which the flaps of the valves project is indicative of the direction of the current. From the disposal of these structures it is correct to infer that the flow is from the depth of the heart to its exterior, thence through channels located in the furrows into the efferent lymphatics leaving the heart, and, after filtering through one or more lymph nodes, into ducts already mentioned that carry it to the venous stream.

A comparison of the lymphatic organization of the lung and heart—two organs so totally dissimilar structurally, functionally, and in the periods of their initial activtiy—shows that the influences which the valves are designed to counteract are situated in the one case outside, and in the other within the organ. While the peculiar distribution of the valves in the lung, as briefly sketched in the introductory paragraph, is the answer to the movements and pressure of the heart, diaphragm, etc., upon it, in the heart the dominating factor is its own musculature, hence the great preponderance of valves on the ventricles.

Similarly, the site of the chief lymph channels in the furrows of the heart like that of the other coronary vessels is without doubt an adaptation to the architectural arrangement of its fascicles and the manner of its pulsation. Analogous to the wringing out of a wet cloth, the kind of contraction brought about by the spiral twist of its muscular bundles—fastened as they are to the fibrous rings of the venous and arterial ostia at the base of the heart and converging at the apex in a vortex—not only effectually evacuates the blood from the ventricular chambers, but also greatly compresses the vessels within their walls. During systole the muscular force together with the pressure of the blood against the endocardium squeeze the lymph from the substance of the heart to its surface. This is facilitated by the relaxation of the pericardial covering and the consequent augmentation in the volume content of its lymph channels occurring when the ventricular diameter diminishes during the beat. It is evident that the extensiveness of the superficial lymphatic plexus is the expression not of any vigorous metabolism within the connective tissue

of the pericardium itself, but of service as a lymph reservoir in close periodic sequence.

The expulsion and outflow of lymph from the heart through the two efferent pathways probably occurs in a continuous stream, for both systole and diastole sustain it, the first because of the shortening of the heart axis from apex to base, the second because of the stretching of the pericardium during the filling of the chambers. Yet during both phases factors arise which also favor backflow in its lymphatics. With the distention of the ascending aorta and the pulmonary artery during ventricular systole and the subsequent closure of their semilunar valves, the adjacent thin-walled lymph vessels would be affected because of their close juxtaposition to them. In the second place, the slackening of the myocardium in the diastolic phase, causing a suction-like action on its vessels, would entail a retrograde motion of the lymph were it not for the interposition of the numerous valvular barriers.

The lymphatics of the heart must be considered as constituting primarily a drainage system carrying away the products of cellular metabolism not selected by the venous capillaries. A few years ago, Pratt (1924) advanced the suggestion that those lymph vessels may serve a nutritive function, imbibing materials from the blood through the endocardium and conveying them to the heart muscle, thus aiding the coronary arterial stream—an hypothesis for which there is little foundation. True, the lacteals absorb foodstuffs through the intestinal lining, yet they do not secrete them again but transport them to the veins for diffusion to the entire organism by the blood stream.

SUMMARY

1. Despite the many papers that have been published on the lymphatics of the heart, much obscurity still prevails concerning their existence in the endocardium and their extent in the myocardium.

2. Because neither the development of the channels in the human heart, nor that and the distribution of their valves have been studied before, the present communication aims to offer information in this matter.

3. At the end of the second lunar month of intrauterine life, two plexiform extensions from the mediastinal lymphatics have entered the base of the heart. One, arising from the upper reaches of the thoracic duct and passing down in front and to the left of the aortic arch, comes to lie between pulmonary artery and ascending aorta and then grows ventral to the latter and along the right coronary artery. The other, a derivative of the pretracheal lymphatic plexus runs behind and to the left of the pulmonary artery to be prolonged along the left coronary artery. Both of these primary channels are permanently retained to constitute the efferent lymph conduits of the heart.

During the third month a net of vessels growing out from them expands rapidly over the periphery of the heart. While that of the ventricular territory eventually becomes intricate and close-meshed, that over the auricular remains less well-developed. Extensions from this superficial or pericardial plexus invade the myocardium to form its plexus.

4. At the end of the third or the beginning of the fourth month of prenatal life, the first valves have their inception in the developing pericardial lymphatic plexus, especially in the main pathways accompanying the coronary vessels; subsequently, they spring up also in the more distant stretches of the network, but in smaller numbers. Their mode of genesis—similar to that in other peripheral lymph channels of the body—varies according to whether they originate at confluences already completed or at confluences just being formed. In one case the valve arises from an endothelial proliferation that encircles the entrance of one vessel into another; in the other, it is produced from the tip or bud of a small vessel that grows at a tangent into the lumen of a bigger vessel.

5. Regardless of the early demands put on the heart in the life of the individual, it acquires its perfect lymphatic organization no earlier than any other organ or region, with the exception of the jugular and mediastinal districts in which the earliest valves make their appearance at two months. In this respect, the heart does not even surpass an organ like the lung which is not called upon to serve until birth.

6. As to distribution, more lymphatic valves are found on the anterior side than on the diaphragmatic side of the heart, at any rate in the fetus. With few exceptions all of these valves occurred on the ventricular portion; for example, of the nearly 300 valves counted in the heart of a 3.8 mo. fetus, not more than four or five were atrial in location. In the depth of the myocardium these structures are absent.

7. Finally, the physiology of the lymph circulation of the heart is discussed: the direction of its flow, the mechanical factors influencing it, and its function.

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COMPARISON OF THE ELECTRICAL AXIS SHOWN BY THE ELECTROCARDIOGRAM WITH ROENTGEN MENSURATION OF THE HEART*

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Determination of the electrical axis (formerly spoken of as the presence or absence of a right or left ventricular preponderance) is part of the routine analysis of electrocardiograms. Deviation of the electrical axis was formerly considered reliable evidence of preponderating enlargement of the right or left ventricle according as the deviation was to the right or left. More recently, however, the work of Cohn[1] and others, and especially that of Herrmann and Wilson,[2] has shown that the electrical axis may be made to deviate from the normal by the position of the heart in the thorax, and by the manner in which the excitation is conducted through the specialized tissue in the ventricles, as well as by change in the relative weights of the right and left ventricles. Herrmann and Wilson compared the electrocardiographic data with the weights of the ventricles separately dissected post-mortem from the remainder of the heart. They found that deviation of the electrical axis and preponderating hypertrophy of right or left ventricle by this method of separate weighing were not in agreement except in instances in which the dissected mass of the ventricles, not the entire heart, weighed in excess of 250 grams. In discussing their work Lewis[3] states that electrical curves cannot be read as indicating preponderating hypertrophy of one or the other ventricle unless independent evidence of very definite cardiac hypertrophy exists; even so, the lie of the heart and the possibility of defective conduction in branches of the A-V bundle may need to be taken into account.

It is my opinion, however, that there is yet a tendency to place too much reliance upon a deviation of the electrical axis as indicative of preponderating hypertrophy of one or the other ventricle. In view of this opinion and the change in the interpretation of the electrical curves which the above-mentioned work demands it was considered desirable to compare the electrical axis with the results of roentgen mensuration of the heart. The latter is considered by most clinicians as the most reliable method of detecting enlargement of the heart in the living patient. Accordingly 100 successive cases, examined in the Heart Laboratory of the Evans Memorial, were selected for checking

*From the Evans Memorial.

of the electrocardiographic evidence of cardiac hypertrophy with the results of roentgen mensuration. All of the roentgen plates were taken at a distance of 6 feet, a suitable distance for teleroentgenography. The electrical axis in the electrocardiograms was determined by the method of Dieuaide.[4]

RESULTS

Number of cases	100
1. Agreement	67
2. Disagreement	23
3. Questionable	10

1. In the 67 cases in which agreement was found the electrical axis and roentgen findings were normal in 60, while in 7 cases the electrocardiogram disclosed left axis deviation and the radiograph enlargement of the heart, more marked of the left ventricle.

2. In the group of 23, in which the data were at variance, the roentgen findings were normal in 21 although axis deviation was present in the electrocardiogram; in two patients the reverse conditions were found. The angle of the axis in the 21 cases measured as follows: −1° to −9°, 2 cases; −10° to −19°, 7 cases; −20° to −29°, 4 cases; −30° to −39°, 3 cases; −40°, 1 case; −57°, 1 case; and +115°, +125°, +150° in the other 3 cases.

3. In the group of 10 patients in whom it was open to question whether the x-ray and electrocardiographic data pertaining to cardiac hypertrophy were in disagreement, the electrical axis was normal in nine and the roentgen findings as follows: symmetrically enlarged, 3; enlarged, especially the left auricle, 1; dilated left auricle, 3; dilated right auricle, 1; and slightly enlarged auricles, 1. In the tenth case the axis measured −12° and the x-ray showed doubtful enlargement, with the heart lying more horizontally due to obesity of the patient.

It is well known that in electrocardiograms taken of enlarged hearts the electrical axis is not deviated to right or left unless the enlargement of the heart is of the type in which either right or left ventricle shows preponderance. Therefore, the normal axis found in the first three of the questionable group merely illustrates a limitation in the electrocardiogram.

In 7 cases the x-ray disclosed enlargement of one or both auricles. The P-wave in Lead II in these cases measured 0.15, 0.15, 0.15, 0.20, 0.20, 0.25, and 0.28 millivolts, respectively. Only the last two figures are suggestive of auricular hypertrophy.

There were 18 cases in which enlargement of the heart was disclosed by x-ray. In 7 of these cases, left axis deviation was present; in 2 the axis was normal. In 4 the enlargement was symmetrical so that the

normal axis in the electrocardiogram could be predicted, and in the remaining 5 cases of this group the roentgen data indicated enlargement of one or both auricles alone; in this last 9 cases the electrical curves are not expected to indicate cardiac enlargement.

Deviation of the electrical axis was present in 29 electrocardiograms, but the roentgen findings indicated enlargement of the heart in but 7 cases. In one other there was a questionable enlargement, and in the remaining 21 cases the x-ray examination disclosed a normal sized heart.

If one eliminates the 60 cases in which there was no enlargement and the 5 in which the enlargement was limited to the auricles, there remain 35 cases in which the electrical axis or the roentgen mensuration indicated enlargement. The percentage of agreement of the two methods of examination is shown in Table I.

Table I

		NUMBER	PER CENT	
Electrocardiogram X-ray	+ +	7	20	
Electrocardiogram X-ray	+ 0	21	60	77%
Electrocardiogram X-ray	0 +	6	17.1	
Doubtful		1	2.9	
Total		35	100	

This work was repeated substituting the "Index"[5] for the electrical axis determined by the method of Dieuaide; the results were about the same by the two methods.

SUMMARY

Deviation of the electrical axis in the electrocardiogram has been shown to be unreliable evidence of preponderating hypertrophy of one or the other ventricle unless the weight of the latter exceeds 250 grams. The position of the heart in the thorax and the possibility of abnormality in the conduction of the impulse through the branches of the bundle of His must be considered.

If the above statements are correct, it is believed that there is yet a tendency to place too great reliance on the electrical curves in the diagnosis of preponderating hypertrophy of one or the other ventricle.

A series of one hundred successive cases have been selected for checking the electrocardiographic evidence of cardiac hypertrophy with the results of roentgen mensuration.

The indications of cardiac enlargement disclosed in the two methods of examination were found to agree in 67 cases, to disagree in 23, and to be questionable in the remaining 10.

In most of the cases in which the results were at variance, the numerical value of the electrical axis indicated a deviation to the right or left although the x-ray disclosed a normal sized heart. Values of the axis as far from the normal (0°–90°) as –40°, –57°, +125°, and +150° were found in this group.

It has long been known that the electrical curves do not disclose symmetrical enlargement of the heart; one ventricle must be enlarged out of proportion to the other.

Enlargement of the auricles, as disclosed in a small group of the radiographs, was not reliably indicated in the electrocardiograms.

In 7 of the 9 cases in which the x-ray showed an asymmetrical enlargement of the heart the electrocardiogram showed a deviation of the electrical axis.

In but 7 of the 29 instances of axis deviation shown in the electrocardiogram did the roentgen examination disclose an enlarged heart.

The percentage of disagreement of the two methods of examination in the 35 cases in which one or the other indicated cardiac enlargement was 77 per cent.

CONCLUSIONS

Deviation of the electrical axis in the electrocardiogram is an unreliable means of determining preponderating hypertrophy of one or the other ventricle.

The interpretation of the character of the waves in an electrocardiogram as indicative of ventricular hypertrophy should require confirmation by the results obtained by other methods of examination, namely, physical and radiographic.

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Department of Clinical Reports

PLEURAL EFFUSION LOCALIZED IN AN INTERLOBAR SPACE*

Report of a Case of Heart Failure Together With Autopsy

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PLEURAL effusion associated with congestive heart failure is observed very frequently, but the localization of fluid in an interlobar space in this state is very unusual. The recognition of the fact that it occurs is important in the differential diagnosis of shadows seen in the x-ray photographs of the chest. It is for this reason that the case of a patient exhibiting this sign is reported.

CASE REPORT

I. P.† (Hospital No. 5869), a female, sixty four years old, was first admitted to hospital on February 12, 1927, complaining of shortness of breath and a sensation of oppression over the heart for six months, and edema of the legs for five days.

The family history was negative.

Past History.—The past history was negative. She had had only measles, mumps, and whooping cough in childhood. She never had acute rheumatic fever, was not subject to attacks of tonsillitis, and was well until the onset of present illness.

Present Illness.—In August, 1926, the patient experienced shortness of breath on exertion. Shortly after this she began to suffer from palpitation; she went to a physician who discovered an affection of the heart, and prescribed digitalis. After taking the drug for several weeks without experiencing improvement she discontinued its use. She also stopped going to the physician. Although she became progressively worse in the next three to four months she did not consult another physician until three days before admission to this hospital. For six months she had experienced at times a feeling of oppression over the precordium. When this sensation was present, she had to sit up in bed to catch her breath. Five days before admission she noticed edema of the feet for the first time. During the next two days this increased, extending up beyond the knees. She then called a physician. She went to bed and was given a milk diet. Although edema decreased very rapidly, her physician advised removal to this hospital.

Physical Examination.—The patient was a well developed, well-preserved woman. She was slightly dyspneic and slightly cyanotic. She coughed occasionally. The pupils were regular and equal; they reacted to light and in accommodation normally. There was slight arcus senilis. There was slight exophthalmos. The eye-grounds were normal except for slight tortuosity of the retinal vessels. All the teeth were present except one molar. The tonsils were enlarged and cryptic. There

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†We wish to thank Dr. Otto V. Huffman for referring this patient to us.

was no tracheal tug. The veins of the neck were distended. On percussion the heart was found to be enlarged. The point of maximal impulse was felt in the sixth interspace, 12.5 cm. from the midsternal line. There were no thrills and no shocks over the precordium. The rhythm of the heart was regular except for occasional ventricular premature contractions; the rate moderately fast. At the point of maximal impulse the first sound was replaced by a soft systolic murmur transmitted to the axilla, the second sound was faint but clear. Over the base the first sound was replaced by a loud rough murmur, the second sound was clear. A diastolic murmur could not be heard. The radial arteries were thickened and slightly tortuous. There was no capillary pulse. There was slight clubbing of the fingers. The systolic blood pressure was 124 mm. of mercury and the diastolic, 70 mm. There was slight dullness at the base of the right lung posteriorly, and the breath sounds were slightly suppressed. Over both bases posteriorly there were many moist bubbling râles extending up as far as the angles of the scapulae. The liver was enlarged. There was free fluid in the abdominal cavity, and slight pitting edema of the legs and ankles.

The count of the white blood cells was 7,400. Of these cells 64 per cent were polymorphonuclear in form. The count of the red blood cells was 4,900,000. The oxygen capacity of the venous blood was 7.56 mm., which is equivalent to 91.5 per cent hemoglobin. The electrocardiogram showed normal sinus rhythm; the conduction time was normal; left ventricular preponderance was present. The Wassermann reaction in the blood was negative. There was a very faint trace of albumin in the urine; the sediment showed a few leucocytes and epithelial cells on microscopical examination. After the patient was free of all signs of heart failure, the phenolsulphonephthalein excretion was 64.8 per cent in two hours and the Van Slyke index of urea excretion was 37.8. A 2-meter x-ray plate of the chest showed the heart to be enlarged. There was slight clouding at both lung bases. On examination of the x-ray photograph of the chest taken at a distance of 42 inches, a shadow was seen in the chest on the right side at the level of the interlobar line. The shadow extended to the ribs laterally but was entirely free from the shadow cast by the heart medially (Fig. 1, January 13, 1927). It measured 5.3 cm. by 5.0 cm. It was sharply outlined. On physical examination it was not possible to detect signs over the area corresponding to the location of this shadow.

The diagnosis* in this patient was: *Etiological:* arteriosclerosis; *Anatomical:* hypertrophy of the heart, chronic myocarditis, mitral insufficiency, aortic roughening, left ventricular preponderance; *Physiological:* normal sinus rhythm, ventricular premature contractions, congestive heart failure.

We thought the shadow in the right chest was cast by a localized collection of fluid due to heart failure. The patient was admitted to hospital on four occasions, and on each of these the shadow was present and appeared to be one of the manifestations of congestive heart failure. It is with the changes in this shadow that this paper is concerned.

Course in Hospital.—While resting in bed and taking 1200 c.c. of fluid a day the edema decreased. At the end of a week, however, her condition became stationary. She was then given digitan (Merck) 1.0 gm.† within twenty-four hours. This produced changes in the T-waves of the electrocardiogram. There was prompt

*This diagnosis conforms to the nomenclature for cardiac diagnosis approved by the American Heart Association. AM. HEART. JOUR., 1926-27, ii, 202.

†One gm. of the preparation was required to alter the T-wave of the electrocardiogram and to reduce the ventricular rate in auricular fibrillation.

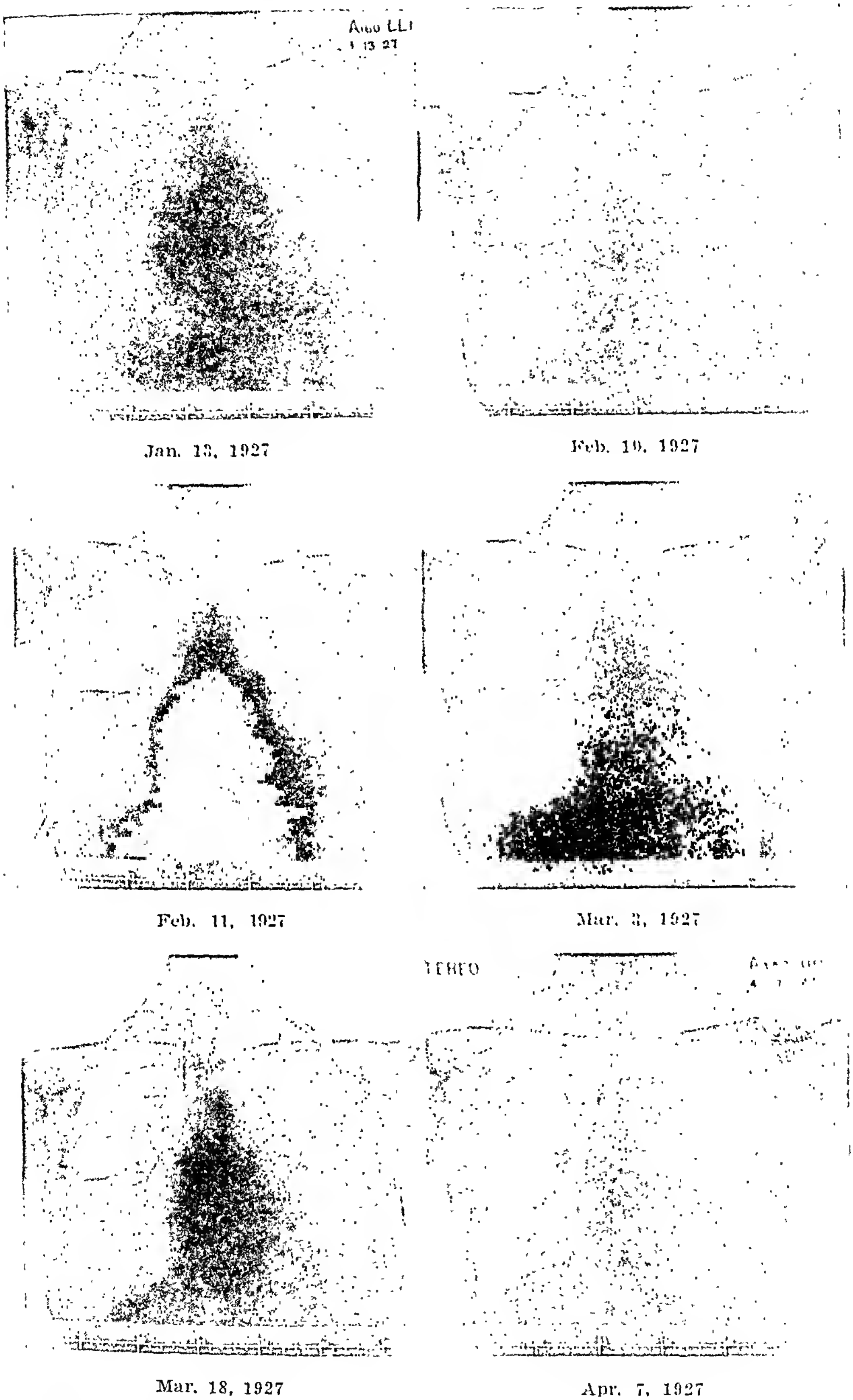

Fig. 1.—In this figure are reproduced x-ray photographs of the chest taken at a distance of 42 inches. These photographs were taken during the patient's first admission to hospital. The series shows a progressive decrease in the size of the shadow in the chest on the right side. In the last photograph (April 7, 1927) it can no longer be seen.

diuresis. In the next three weeks the dyspnea decreased, the edema disappeared, the ascites decreased, the râles decreased in number, and the liver could no longer be felt. During this time the weight decreased from 54.2 kg. to 47.7 kg., about half of this loss occurring in the course of the first four or five days. During this time the size of the shadow in the right chest did not change.

On the night of February 8, the patient complained of persistent precordial pain. There were no new signs on physical examination. On the evening of February 9, the temperature rose to 102.4° F. (rectal). She was apprehensive and looked ill. She complained of shortness of breath. She coughed. The leucocyte count was 6,000. A blood culture taken at this time remained sterile. The sputum contained no pathogenic organisms by culture or on mouse inoculation. There was no change in the form of the electrocardiogram. On February 10 the temperature rose to 103.7° F., but fell again to normal and remained there. An x-ray photograph taken on February 10 showed that the shadow in the right chest had decreased very much in size (Fig. 1, February 10, 1927), and on February 11 (Fig. 1) and 13 decreased still further. On February 14 the temperature rose again to 101.4° F., and on February 15 the count of the white cells was 11,000. For the next two weeks there were occasional slight rises in temperature above normal. On February 15 and 17 the shadow was still smaller. On February 18 the patient received digitan, 1.0 gm. within twenty-four hours. This was followed by a slight decrease in body weight. By February 23 she was coughing less frequently and ascites had disappeared. There were still a few râles at the pulmonary bases posteriorly. The shadow was seen to be still decreasing in size when photographs were made on February 21, 23, and 26. On February 28 râles could no longer be heard. An x-ray photograph taken on March 3 revealed that the shadow was reduced to a narrow band (Fig. 1). By March 10 the band was still narrower, and by April 7 the shadow had disappeared. The patient was discharged on April 9. She was directed to continue taking digitalis and to limit her fluid intake to 1200 c.c. per day.

On April 27, the patient returned to the hospital for examination. The shadow was again present in the right side of the chest. She had been indulging in more exertion than had been recommended.

On May 7 the shadow had increased still further in size; the patient was readmitted to the hospital for the second time. Except for enlargement of the liver there were no other signs of heart failure. Diuresis occurred promptly when she was given digitalis; the size of the shadow became smaller and finally disappeared (June 1). The patient was discharged. During this admission a rise in temperature did not occur.

On July 8 the shadow had returned again. There were no other signs of heart failure except the presence of the shadow. She was advised to continue taking digitalis and to limit her activities during the summer. On October 14 the shadow was larger. The rhythm of the heart had changed to rapid auricular fibrillation. She went to bed at home and began taking digitalis. On October 18 she was readmitted for the third time. There was slight congestion at the bases of the lungs, the liver was enlarged and there was slight edema of the extremities. Auricular fibrillation was still present. The shadow was larger. She was given digitalis. The volume of urine increased; she became free of the signs of congestive heart failure, and the shadow practically disappeared. She left the hospital on November 8.

The patient was readmitted to the hospital on March 6, 1928, for the fourth time. Heart failure had proceeded much further than on previous admissions. There was marked edema of the extremities extending up to the waist, as well as marked ascites, enlargement of the liver, congestion of the lungs, marked cyanosis

and dyspnea. She had been in this state since January, 1928, but did not wish to enter the hospital. Auricular fibrillation was still present. X-ray examination showed that the shadow was again present. She had been taking digitalis and the ventricular rate was moderately slow. She was given 1200 c.c. of fluid per day for a few days, but did not improve nor did diuresis occur. She was given theocalcin (Merck), 4.5 gm. a day. On the second day of its administration diuresis began. In nine days she lost more than 7.0 kg.; the diuresis at times was more than 3000 c.c. per day. Edema and ascites decreased. There was, however, no change in the size of the shadow. Theocalcin then became less effective and was discontinued. She had not been given digitalis since admission and the ventricular rate was more rapid. The administration of digitan, 1.2 gm. within twenty-four hours, was followed by decrease in ventricular rate; there was, however, no increase in the amount of urine. We continued to give small doses of digitalis in order to keep the ventricular rate slow. During the next weeks theocalcin was given as long as diuresis occurred; when the volume of urine decreased, it was discontinued for a few days. She lost weight and became almost free of the signs of congestive heart failure. The patient now exhibited very frequent ventricular premature contractions. Later, long paroxysms of ventricular paroxysmal tachycardia occurred, while in the intervals between paroxysms there were many ventricular premature contractions. Quinidine was given, but frequent ventricular premature contractions continued to be present interspersed with long runs of ventricular paroxysmal tachycardia. The rapid rate could not be controlled either by the omission of or by the administration of digitalis. The patient grew worse rapidly and died on May 3, 1928. In the x-ray photograph taken on April 26, 1928, the shadow was still present and its size was unchanged.

SUMMARY OF AUTOPSY

Macroscopical Diagnosis.—Calcification and stenosis of the aortic valves; malformation of the aortic valves; cardiac hypertrophy; advanced atherosclerosis of the aorta; moderate atheromatosis of the aortic cusp of the mitral valve and of the coronary vessels; atherosclerosis and infarcts of the kidneys; ascites; edema of the legs and intestines; serous pericarditis; serofibrinous pleurisy of the left cavity with few old adhesions; *obliteration of the right pleural cavity with the exception of a small space between the upper and middle, lobes, which was filled with serofibrinous fluid;* pleural induration over both apices; osteoporosis of the sternum.

Microscopical Diagnosis—Heart: Calcification of the aortic valves; old endocarditis (?) and pericarditis of the left auricle; atheromatosis of the aortic cusp of the mitral valve. Aorta: Calcifying atherosclerosis of the intima in the thoracic portion and of intima and media in the abdominal portion of the aorta. Renal arteries: Calcifying atherosclerosis. Lungs: Adhesive pleurisy of the right cavity; purulofibrinous pleurisy in the space between the right upper and middle lobes; serofibrinous pleurisy of the left pleural cavity with purulent lymphangitis; chronic passive congestion; arteriosclerosis. Liver: Atrophic induration and chronic passive congestion. Kidneys: Arteriosclerosis; healed infarcts; passive congestion. Spleen: Passive congestion. Adrenals: Passive congestion. Mesenteric lymph nodes: Sinus catarrh.

Attention at autopsy naturally centered on the right pleural cavity, but the heart was also found to be of especial interest.* The right

*The complete autopsy report and description of the heart will be reported more fully in another paper (Ehrich and Stewart).

lung was adherent throughout to the parietal pleura (Fig. 2), so that the right pleural cavity was completely obliterated. To remove the lung it was necessary to dissect the parietal pleura from the chest wall. The three lobes were adherent to each other, except for a small area at the lateral margin between the upper and middle lobes (Fig. 2). This cavity was filled with pale yellow fluid which was slightly turbid. This location corresponded to that of the shadow which was

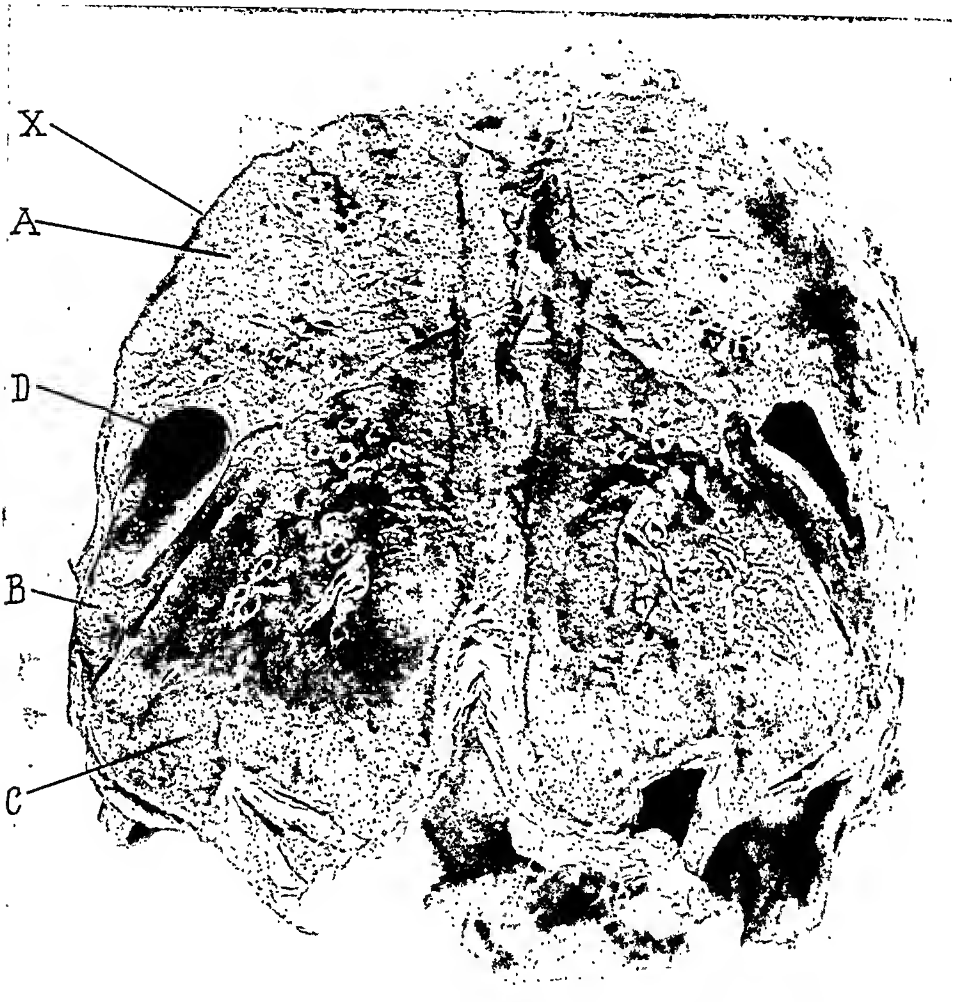

Fig. 2.—In this figure is reproduced a photograph of the right lung on section. *A* is the upper, *B*, the middle, and *C*, the lower lobe. The space (*D*) between the upper and middle lobes was filled with fluid. The visceral and parietal pleurae were adherent and formed one thick layer *X*.

seen in the x-ray photographs of the chest. On microscopical examination the pleura of the right lung was thickened and connective tissue was abundant. It was adherent to the parietal pleura. The pleura lining the cavity between the upper and middle lobes was thickened and contained large numbers of round cells and polymorphonuclear leucocytes. It was covered with masses of fibroid tissue in which were many polymorphonuclear leucocytes and a smaller number of round

cells. A number of gram-positive cocci were found here, lying partly in couples and partly in chains.

The heart was very much enlarged. There was atheromatosis of the aortic cusp of the mitral valve. There was marked calcification of the aortic valves and the aortic opening was almost obstructed by large rough calcified masses.

The lesion of the heart was apparently that of primary atherosclerosis. The right pleural cavity was entirely obliterated, with the exception of a small space between the upper and middle lobes of the right lung, which was filled with fluid. The gross and microscopical examination did not throw light on the etiological process which was responsible for this state.

COMMENT

The shadow just described was thought to be due to a localized collection of pleural effusion in congestive heart failure, the fluid occupying the space between the upper and middle lobes of the right lung. The position in the x-ray photographs corresponded with this location. Although pleural effusion is one of the most frequent manifestations of congestive heart failure, localization, such as occurred in this patient, is rare. The reason for the sharp localization could not be definitely known when the patient first came under observation. The shadow could, of course, have been caused only by fluid since it disappeared so completely and so quickly and recurred with each attack of heart failure. Adhesion of the visceral and parietal layers of the pleura left, it was thought, only a small free space between the two lobes in which fluid could collect.

When the shadow was first discovered, it was difficult to decide what was casting it. The smoothness of its outline and the absence of metastatic foci were against its being due to a newgrowth. There was no evidence of the presence of pulmonary tuberculosis upon which a diagnosis of localized pleurisy with effusion could be made. The x-ray photographs were not incompatible with a diagnosis of localized empyema. There was, however, nothing in the past history suggesting pulmonary infection which might have had this sequela. In addition the disappearance of the shadow later and its reappearance with each attack of heart failure made this diagnosis seem unlikely. That it was due to fluid, accumulating during congestive heart failure, seemed then to be the most likely diagnosis. It did not seem justifiable at any time to aspirate the fluid for examination. The shadow first began to decrease in size coincident with an attack of precordial pain which was followed by fever. The two events appeared to be unassociated, though it was, of course, impossible to be certain of it. There was slight leucocytosis. During fever the patient had slight persistent cough and for this reason respiratory infection had to be considered.

X-ray photographs did not disclose evidence of bronchopneumonia. Bacteriological studies were also negative. In spite of the absence of pericardial friction rub and of changes in the electrocardiogram, a diagnosis of coronary occlusion was made. This was based on the history of cardiac pain, and the presence of fever and leucocytosis.

In the second and third admissions heart failure was not so severe as on the first; the shadow disappeared more quickly and without a rise in temperature, which occurred, as has already been said, coincident with its decrease in size during that admission. After observing the patient and the changes in the shadow on three occasions it was thought that the shadow could only have been cast by fluid, the presence of which was due to congestive heart failure. That it was fluid was definitely settled when the fourth attack of heart failure terminated fatally and the patient came to autopsy. The presence of fluid in the interlobar space and the obliteration of the right pleural cavity by adherence of the visceral and parietal layers of the pleura were, just as had been supposed, the pathological conditions. It was not possible to discover the underlying pathological process responsible for complete obliteration of the right pleural cavity. Why it occurred in this form rather than in the somewhat more common form of dense fibrous bands also cannot be explained. The patient did not recall having had an illness before the onset of the present one. The adhesion of the two layers of the pleura must already have occurred before the onset of the first attack of heart failure, since the shadow was discovered a few days after its onset.

Between the second and third admission the mechanism of the heart changed to auricular fibrillation. Because of enlargement of the heart, it seemed unwise to attempt to restore the normal rhythm with quinidine. After each attack of heart failure from which the patient recovered she found it necessary to lead life on a slightly lower level. At the time of the first admission the area of the heart (traced from x-ray photographs taken at a distance of 2 meters) measured 152.8 sq. cm., and on discharge 132.5 sq. cm., a decrease in size of 14 per cent having taken place. The maximum and the minimum sizes of the heart during this admission were 175.0 sq. cm. (February 4, 1927) and 130.0 sq. cm. (April 1, 1927) respectively. At the time of the second admission the area of the heart was 171.6 sq. cm., and on discharge, 144.4 sq. cm., that is to say a decrease of 16 per cent occurred. The heart remained, however, larger than it was at the time of the first discharge (132.5 sq. cm.). At the time of the third admission the area of the heart was 169.7 sq. cm., and on discharge, 148.4 sq. cm., a decrease of 13 per cent. The heart was again larger than it had been when the patient was discharged the first and second times. At the time of the fourth admission, March 6, 1928, the area was 157.8 sq. cm. and the smallest

recorded was 150.2 sq. cm. (April 4, 1928). In the last photograph taken on April 26, 1928, it was 160.8 sq. cm.

In studying the clinical course of the patient the rapidity with which the disease ran its course is striking. Before the first attack the patient had a few symptoms of congestive failure for six months, but afterward there were 4 attacks within eleven months. The last attack terminated fatally, fifteen months after onset and twenty-one months after the onest of the first cardiac symptoms. During fifteen months she was confined to hospital approximately six and a half months, and recovered satisfactorily from each of the first three attacks.

SUMMARY

A case is presented in which during each of 4 attacks of congestive heart failure a shadow was observed in x-ray photographs of the chest, the shadow seeming to occupy the space between the upper and middle lobes of the right lung. The shadow was thought to be cast by fluid, the amount being too small to give signs on physical examination. With disappearance of signs of heart failure the shadow also disappeared. The patient succumbed to the fourth attack of failure and autopsy examination revealed (as we had supposed it would) a small pleural effusion confined to the space between the upper and middle lobes of the right lung, adhesive pleurisy completely obliterating the remainder of the right pleural cavity. The etiology of the adhesive pleurisy was not discovered. The etiology of the heart disease was apparently primary atherosclerosis.

Department of Reviews and Abstracts

Selected Abstracts

Haberlandt, L.: Preparation and Demonstration of the Heart Hormone. Hdb. d. Biol. Arbeits meth., 1928, Section 5, Part 8, Heft 2, p. 237.

The author prepares his heart hormone by immersing the sinus venosus and great veins of two frogs (Rena Esculenta) in 1 c.c. of Ringer's solution. The extract may be equally obtained from the sinus node or the A-V bundle. When perfused through the isolated frog's ventricle by Straub's cannula, acceleration and increased amplitude of the beat will occur if the heart is hypo-dynamic or if it has stopped, pulsations will be initiated.

The extract employed differed from the accelerator material described by Loewi in not being destroyed by fluorescence or ultraviolet light. It does not resemble adrenalin as it produces vasodilation rather than vasoconstriction. The hormone may be extracted with alcohol, less easily with chloroform and not at all with ether. The aqueous extract seems to be the more suitable. The hormone is heat resistant and is adsorbed by charcoal.

Similar work done on warm blooded animals shows that an extract prepared in Locke's solution from the right auricle in dogs produced an increase in the number and amplitude of beats in rabbits' hearts.

The hormone does not seem to be genus specific and may be obtained from the entire conducting system of the heart. The author quotes the work of Ryland and De Moor, Kemal, Mouchet and others, who have worked on similar lines.

Cohn, Alfred E., and Stewart, Harold J.: The Relation Between Cardiac Size and Cardiac Output per Minute Following the Administration of Digitalis in Normal Dogs. Jour. Clin. Invest., 1928, vi, 53.

Following the administration of digitalis in normal dogs in so-called therapeutic amounts, the following effects were observed: the form of the T-wave in the electrocardiogram changed; cardiac output as determined by the principle of Fick was decreased; the size of the heart decreased, and the height of ventricular excursions increased. These excursions were determined by the authors' method of photographing the motion of points of the hearts' borders by casting shadows of these points made by roentgen rays upon moving films.

When digitalis was excreted all these measurements returned toward normal. The cardiac output often became greater than the initial value.

The authors conclude that digitalis within the first twenty-four hours decreases the output. The cardiac output which obtains at any later instant is the net result of the workings of two opposing factors. The first of these effects increases cardiac tone and results in decrease in the size of the heart. It is due to this action that cardiac output tends to decrease. The second effect increases ventricular contraction and tends to increase cardiac output. If cardiac size is not smaller than a critical value, increase in ventricular contraction overbalances decrease in size so that cardiac output increases beyond the beginning value.

Cohn, Alfred E. and Stewart, Harold J.: The Relation Between Cardiac Size and Cardiac Output per Minute Following the Administration of Digitalis in Dogs in Which the Heart is Enlarged. Jour. Clin. Invest., 1928, vi, 79.

The authors have studied the effect of digitalis upon the cardiac output, cardiac size and ventricular contraction of dogs with enlarged hearts, but without signs of heart failure.

The effect of digitalis on these hearts is the same whether they are normal in size or enlarged. They point out that it is still necessary to learn whether enlargement resulting from mechanical embarrassment requires differentiation from enlargement due to underlying disease in which edema is a conspicuous phenomenon.

Smith, W. Carter, Burwell, C. Sidney, and DeVite, Michael J.: The Effect of Atropine Upon the Output of the Hearts of Normal Men. Jour. Clin. Invest., 1928, vi, 237.

Atropine administered intravenously to normal men increases the rate of the heart relatively much more than the output of the heart per minute and thus produces a diminution in the output of the heart per beat. There is a relatively small rise in cardiac output per minute and no change in pulse pressure in metabolic rate following the use of the drug.

The absence of constant changes in the blood pressure levels indicates the extraordinary adjustability of a circulatory mechanism which can suffer a large sudden increase in pumping strokes per minute without alteration of pressure. Indeed it appears that heart rate, cardiac output, or blood pressure may change within limits, without involving each other, so perfect and instant are the compensatory mechanisms.

Burwell, C. Sidney, and Robinson, G. Canby: A Note on the Cardiac Output of a Single Individual Observed Over a Period of Five Years. Jour. Clin. Invest., 1928, vi, 247.

In 1924 the authors reported the results of a study of the output of the heart in normal resting adults and at that time noted that two of the subjects differed in the degree of variation exhibited by their cardiac output at different times but under identical circumstances. In one of the subjects five measurements scattered over a year varied only from 3700 to 3960 c.c. per minute.

The first group of measurements on this subject was made by the authors' method. Since that time a second series of determinations have been made by the method of Bock, Field, Gildea and Lathrop. The output of the heart remained relatively unchanged throughout the whole period. This general agreement constituted not only a demonstration of the degree of perfection of physiological regulation but also impressive evidence of the agreement in this subject of two quite different methods of measuring the output of the heart.

Markel, Albert G., and Pardee, Harold E. B.: The Correlation of Electrocardiographic and Necropsy Findings. Am. Jour. Med. Sc., 1928, clxxvi, 479.

The object of this investigation is an attempt to correlate the form of the ventricular waves of the electrocardiogram with the condition of the heart at necropsy. For this purpose, a study was made of a series of 10 cases in the wards of the New York Hospital. Two cases are presented with microscopically normal muscle and no significant abnormality of the electrocardiogram. Evidence is also presented that a curve showing notched QRS complexes with a slightly

abnormal duration and an abnormal T-wave represents the definite microscopic abnormality but one less severe than indicated by the curves of bundle-branch block or intraventricular block.

Birkhaug, Konrad E.: Allergic Reactions with a Toxin-Producing Strain of the Nonmethemoglobin-Forming Streptococcus Isolated from Rheumatic Fever. Jour. Infect. Dis., 1928, xliii, 280.

Guinea pigs and rabbits sensitized to the non-methemoglobin-forming streptococcus isolated from rheumatic fever may be rendered cutaneously hypersensitive to filtrates of cultures of this organism. A brief period of specificity in the sensitive state is recorded. This period is shortly followed by a sensitive state that is non-specific. During this phase of the cutaneous reactions, the allergenic property of the filtrate can be nullified completely with specific antiserums. After the end of the cutaneous allergy of this first phase, continued sensitization of the animals with living non-methemoglobin-forming streptococci produces the reappearance of cutaneous allergy. During the second phase, the reactions of allergy are nonspecific and the allergic principle of the filtrate is nonneutralizable with specific antiserums. For this phase, filtrates heated at 98° C. for four hours are not inactivated as allergic substances. Heterogeneity in the cutaneous responses of patients with rheumatic fever to filtrates of the non-methemoglobin-forming streptococcus and to certain strains of Streptococcus viridans might be explained on the basis of prolonged sensitization to any one dominant strain of the non-hemolytic streptococci. Desensitization of bacterially hyperallergic guinea pigs and rabbits was accomplished during the second phase of cutaneous allergy by intracardial or intravenous injections of bacterial filtrates.

Fischer, Robert: Clinical Studies of Paroxysmal Tachycardia and Parasystole. Wien. Arch. f. Klin. Med., 1928, xvi, 137.

In this paper an attempt was made to analyze two rare cases of tachycardia. In the first case of decompensated hypertension the paroxysmal tachycardia was caused by a reciprocal rhythm. Superventricular extrasystoles producing the attack caused a delay in conduction and a longitudinal dissociation in the His bundle allowing the normal impulse to return to the auricle from where a new impulse reaches the ventricle. Parasympathetic stimulation stopped this mechanism especially toward the end of the attack, so that longer periods of *normal* heart rhythm were present.

The second case showed a marked hypertrophy of the left ventricle and a certain number of extrasystoles alternated regularly with 2 normal systoles. The name "intermittierende tachycardie" was given to this condition. The case was analyzed according to the method of Kaufmann and Rothberger and the possible explanations for this phenomenon were discussed.

Blumgart, Herrmann L., and Weiss, Soma: Clinical Studies on the Velocity of Blood Flow. XI. The Pulmonary Circulation Time, the Minute Volume Blood Flow Through the Lungs, and the Quantity of Blood in the Lungs. Jour. Clin. Invest., 1928, vi, 103.

Measurements of both the minute volume flow through the lungs and the pulmonary circulation time have been made in 17 normal persons and the approximate amount of the blood in the lungs has been calculated. The average calculated amount of blood in the lungs was 984 c.c. or approximately 21 per cent of the total blood volume. The quantity varies considerably in different individuals.

The results indicate that the pulmonary circulation time is an index of the mean time consumed by the blood flow through the lungs.

The observations suggest that in normal persons the available pulmonary pathways are approximately equal.

Normal variations in the pulmonary circulation time are not related to corresponding normal variations in the minute volume blood flow through the lungs.

Chadwick, R. Taylor.: The Levulose Tolerance of Convalescent Children with Special Reference to Rheumatism. Arch. Dis. Childhood, 1928, iii, 179.

Levulose tolerance tests were done in a group of 35 children, 9 of whom were regarded as controls. The remaining 26 were rheumatic and were grouped according to the presence or absence of a heart lesion and according as to whether the process was active or quiescent.

The dose of levulose used varied between 20 to 30 gm. and the Hagedorn-Jensen method of estimating the blood sugar was used.

The control cases which were well showed either no change or a very slight rise in the blood sugar. The same occurred in cases of chorea who did not have cardiac involvement.

Levulose intolerance was demonstrable in cases of chorea with heart involvement and in acute rheumatic fever whether carditis was or was not present. With recovery the tolerance improved.

This intolerance is thought probably to be due to toxic absorption from a rheumatic focus.

Poynton, F. J., and Sheldon, W. P. H.: Coarctation of the Aorta with Ulcerative Aortitis. Arch. Dis. Childhood, 1928, iii, 191.

The authors report a case of coarctation of the adult type occurring in a boy of eight years. On examination a systolic murmur was audible loudest in the third and fourth intercostal spaces midway between sternal edge and right nipple; a large pulsating external mammary artery was present and blood culture showed a hemolytic streptococcus.

At autopsy the heart was slightly enlarged and the constriction in the aorta occurred just beyond the origin of the subclavian artery and beyond this an ulcer was present.

Other anomalies present included a bicuspid aortic valve and a common origin of the innominate and left common carotid arteries. The ductus arteriosus as in most cases of the adult form of the condition was closed.

The authors review 4 other cases of coarctation from the literature where an infectious aortitis was fatal.

Rosler, H.: Contributions to the Conception of Congenital Heart Disease. 1. X-ray Findings in Congenital Malformations of the Heart and the Vessels. Wien. Arch. f. Inn. Med., 1928, xxv, 487.

The author shows that positive x-ray findings were obtained in about 85 per cent of the 68 cases under his observation. In 50 per cent of these cases the x-ray picture was of definite value for the diagnosis of a malformation.

Rosler, H. L.: Contributions to the Conception of Congenital Heart Disease. 2. Investigation on the Etiology. Wien. Arch. f. Inn. Med., 1928, xxv, 495.

Sixty cases were followed up from this point of view. Thirty-two were male, 28 female. In none of these cases could a familial occurrence of congenital heart disease be found. In 7 cases there was positive evidence of rheumatic heart disease

in the family. Trauma, physical or mental disease of the parents during cohabitation or pregnancy did not contribute to the frequency of the malformations. The toxic effects of alcohol were thought responsible in 8 cases, but the amount of material was so small that the figures are within the limits of statistical error. The same was true for cases in which consanguinity of the parents was found. (6 cases.) A relation between congenital lues and congenital heart disease could not be established.

Rosler, H.: Contributions to the Conception of Congenital Heart Disease. 3. Observations on a Case of Pulmonary Stenosis. Wien. Arch. f. Inn. Med., 1928, xxv, 507.

The author gives an extensive report of the clinical, radiological and postmortem findings in a case in which the diagnosis had been made of pulmonary stenosis combined with defect of the interventricular septum. The autopsy showed that the stenosis of the pulmonary artery was caused by a diaphragm below the level of the valves with the remains of an old endocarditis. Other malformations present included congenital luxation of the hip and anomalous cervical vertebrae. An analysis of the discrepancies between clinical and autopsy observations was made.

Rosler, H.: Contributions to the Conception of Congenital Heart Disease. 4. Observations in Two Cases of Stenosis of the Isthmus of the Aorta. Wien. Arch. f. Inn. Med., 1928, xxv, 521.

Two typical cases of stenosis of the isthmus of the aorta, one of which could be confirmed by autopsy are described and the clinical radiological and anatomical picture of the condition is discussed.

Fleming, G. B., and Stevenson, Mary M.: Heart Block Associated with Congenital Malformation of the Heart. Arch. Dis. Childhood, 1928, iii, 221.

The authors report two cases of heart block associated with congenital malformation of the heart.

The first case was a male child of three and one-half years. The classical symptoms of congenital heart disease were not present but the heart was enlarged, a systolic murmur being audible over the precordium and transmitted to the axilla and right shoulder. The pulse varied between 30 and 60 and the electrocardiogram showed a complete and permanent auricular ventricular dissociation, the auricles beating between 80 and 125 and the ventricles between 35 and 50. The block was unaffected by atropine, adrenalin and exertion.

The second case is that of a girl eight years of age, who showed mental and physical retardation. Cyanosis, clubbing and polycythemia were present and fainting spells were frequent. The heart was enlarged. A systolic murmur was present over the precordium especially loud in the left third intercostal space and transmitted to the left third intercostal space and transmitted to the left clavicle and scapula. The "Q" wave was present. None of the measures attempted abolished the block but after exertion regular ectopic beats followed each normal beat, and during the compensatory pause, the blocked auricular beat was visible.

The authors discuss the pathology and state that the block per se causes little disability, any symptoms present being due to the presence of other anomalies.

Lampard, M. E.: Heart Block Associated with Congenital Heart Disease. Arch. Dis. Childhood, 1928, iii, 212.

The author reports a case of complete heart block in a boy of six years. The congenital nature of the lesion was surmised, although the author mentions the possibility of diphtheritic origin. The heart was enlarged and globular in shape, the ventricular rate being 48, the auricular 75. The blood pressure measured 116 systolic and 64 diastolic. A thrill and murmur were present over the pulmonic area and a diastolic bruit was later audible over the precordium. No clubbing, cyanosis or polycythemia were present.

The author summarizes the thirty cases reported in the literature and discusses the probable pathology of the condition. He concludes that the lesion is probably due, not so much to a hole in the ventricular septum but to the presence of fibrous tissue causing pressure on the His bundle. When the bundle runs on the edge of the septal defect it may be damaged by infectious processes.

White, Paul D.: The Effect of Strain on the Heart. New Eng. Jour. Med., 1928, cxcix, 801.

In a discussion of this important subject the author divides heart strain as due to intrinsic or extrinsic factors. The intrinsic factors consist of structural defects or lesions in the heart and disorders of rhythm. The extrinsic factors causing heart strain are of far less importance than the intrinsic ones with two exceptions. These exceptions are hypertension and hyperthyroidism.

These various points are discussed from a very conservative viewpoint and should prove of value in furthering our ideas as to what may be expected in an individual patient complaining of symptoms from his heart.

Ziskin, Thomas: The Electrocardiogram in Hypertension. Arch. Int. Med., 1928, xlii, 512.

A study was made of 100 consecutive patients with hypertension to determine the significance of electrocardiographic observations in hypertensive heart disease. Sixty-three of these patients showed some abnormality. These consisted of extrasystoles, delay in conduction, inversion in T-wave and evidence of left ventricular preponderance. The signs of left ventricular preponderance were present in only 44 of the 100 patients.

The author has investigated factors that determine the appearance of these signs of ventricular preponderance in patients with hypertensive heart disease.

Christian, Henry A.: Chronic Nonvalvular Disease of the Heart. Jour. Am. Med. Assn., 1928, xci, 549.

The author discusses chronic nonvalvular disease of the heart in contrast to chronic valvular heart disease in patients with symptoms of cardiac derangement in whom study does not reveal evidence of any lesions of the endocardium or pericardium. He points out that the myocardium is responsible in a great many patients for the symptoms of cardiac failure even though the muscle itself seems normally nourished and devoid of evidences of degeneration or inflammation.

Chronic myocardial insufficiency or chronic myocarditis is a very serious disabling disease of the heart and along with myocardial fatigue we find in this paper is the cause of cardiac symptoms in an extremely large proportion of cardiac patients.

This paper will be welcome to those physicians who find large numbers of patients of this type in their practice. Various features of this important condition are discussed.

Howard, C. P., and Mills, E. S.: Acute Articular Rheumatism and Other Members of the Rheumatic Cycle. Canad. Med. Assn. Jour., 1928, xix, 403.

The authors have studied a group of 241 patients admitted to the Montreal General Hospital for acute articular rheumatism or its complications during three years time. This group of patients represents 5 per cent of the total admissions during this time.

Arthritis occurred in 55.7 per cent under observation though there was a history of arthritis at some period of the disease in 80 per cent. Of the cardiac manifestations, there was an acute or chronic endocarditis in 68 per cent, myocarditis in 41 per cent and pericarditis in 17 per cent. Tonsillitis occurred in 46 per cent; acute or chronic pleurisy was surprisingly frequent, occurring in 15.3 per cent. The average hospital stay of the patient was six weeks. 20 per cent were discharged as cured, 64 per cent as improved and 5 per cent as unimproved. There was a mortality of 9 per cent.

Barr, David P.: Exercise in Cardiac Disease. Jour. Am. Med. Assn., 1928, xci, 1354.

The author emphasizes several principles which have a bearing on our conception of exercise in cardiac disease, reviewing the literature of our present knowledge.

In the study of muscular exertion two kinds of inadequacy must be considered separately. The first of these is a failure to supply the tissues with sufficient blood and oxygen. This may occur in any person at all, from the most highly trained athlete to the severely decompensated cardiac patient, but with different amounts of work. Whenever it occurs there is an oxygen debt, an accumulation of lactic acid and an exaggerated pulmonary response. Intrinsically it does not imply any abnormality, or cardiac weakness. The second form may be designated congestive heart failure and arises because the cardiac output does not keep pace with the inflow of blood to the heart. It is usually if not always dependent on myocardial insufficiency or disease. It occurs earlier and with less exertion when a mechanical factor, such as mitral stenosis, is also present.

In normal persons, exercise may be attempted in which sufficient supply of blood and oxygen to the tissues is impossible. Congestive cardiac failure, however, does not occur because respiratory factors limit the exercise before the maximum cardiac response has been attained. The patient with heart disease incurs an oxygen debt from more trivial causes. Dyspnea occurs earlier and is more severe. As in normal persons, the lungs may be the limiting factor and may protect the heart. The protection, however, may be insufficient and congestive heart failure may result.

In both normal persons and cardiac patients, dyspnea is the greatest safeguard against the possibility of heart strain and cardiac failure. Patients who have mechanical factors such as mitral stenosis have greater dyspnea and are more protected than those patients in whom this factor is absent. In patients with syphilitic disease of the aortic valve, with chronic hypertension and perhaps with myocardial defects, it may not be safe to accept dyspnea as the warning signal for the control of exercise. The observance of other symptoms or, indeed, an entirely arbitrary limitation of exertion may be necessary to furnish sufficient protection.

Levine, Samuel A., Fulton, Marshall N.: The Relation of Hypertension to Mitral Stenosis. Am. Jour. Med. Sc., 1928, clxxvi, 465.

To confirm an impression that patients with mitral stenosis over the age of forty-five years commonly have an elevated blood pressure, the authors have studied 762 cases of mitral stenosis admitted to the wards of the Peter Bent Brigham

Hospital, between 1913 and 1927 and those seen in private practice during the past eight years. The cases have been divided arbitrarily according to age, as those over or under forty-five years. As those with hypertension, all cases having a systolic pressure of 105 mm. or over and a diastolic of 90 mm. or over have been included. Only those cases have been included in which the mitral valve alone was involved. Only cases were included in the hypertensive group in which the physical findings during life were sufficient to make a diagnosis of mitral stenosis quite certain.

Of the total of 762 cases, 159, 21 per cent were over forty-five years of age. Only 17 of these were examined after death. They all showed definite mitral stenosis, some with a mere crescentic slit, others with a less marked degree.

The study of these cases seems to indicate that with advancing years patients with mitral stenosis have vascular hypertension with much greater frequency than the average population. Out of 159 cases there were 92 or 58 per cent with hypertension. Mitral stenosis of itself tends to have a blood pressure slightly lower than normal. Evidence is presented from the study that the mitral stenosis found in older patients is not a part of the general sclerotic process alone, but must be rheumatic in origin in as much as these patients have the same incidence of a previous history of rheumatic fever or chorea as do the younger patients.

The authors feel the unusual association of hypertension with mitral stenosis results from a particular vulnerability that these patients have both for the infectious and degenerative types of vascular disease.

There is some evidence from this study to show that vascular hypertension exercises a beneficial effect on cases of mitral stenosis. This can be explained on the basis that the increased load on the left ventricle as a result of the hypertension tends to keep this cavity dilated and to stretch the mitral ring and thereby to delay the contraction resulting from the mitral stenosis. It also tends to obviate the imbalance of the two ventricles.

Schneier, Joseph: The Indications for Tonsillectomy in Arthritis and So-called Rheumatic Diseases. Wien. Arch. f. Klin. Med., 1928, xvi, 119.

In 39 cases of acute rheumatic fever in adults followed over a period of from two to sixteen years after tonsillectomy, 31 were cured. In secondary chronic arthritis (arthritis and myalgia following acute rheumatic fever) out of 43 cases, 18 were cured, 10 improved and 15 did not show improvement. In all the other forms of "so-called" rheumatic disease tonsillectomy did not improve the condition.

The author proposes to do a tonsillectomy after the acute stage in acute rheumatic fever and in secondary chronic arthritis independent of the clinical appearance of the tonsils.

Farnum, Waldo B.: The Effect of Tonsillectomy on Existing Cardiac Disease in Adults. Am. Jour. of Med. Sc., 1928, clxxvi, 474.

This study has particularly to do with the results of tonsillectomy on a pre-existing endocarditis. The cases used for the investigation were 526 patients followed in the adult cardiac clinic at St. Luke's Hospital, New York for from two weeks to nine years. The author concludes that tonsillectomy although carried out under as nearly ideal conditions as may be obtained may initiate an attack of acute rheumatic polyarthritis in a certain number of cases, and further an actual spread of endocardial or myocardial infection.

The recurrence of sore throat may not be avoided since infection elsewhere in the nasopharynx may recur. With these recurrences, there may be oftentimes attacks of acute rheumatic polyarthritis and renewed cardiac involvement. Tonsillectomy

in this group of cases does not seem to have a very great effect on the recurrence of chorea, as about 20 per cent recurred in both the tonsillectomized and the non-tonsillectomized.

It seems fair to conclude from these observations that in adults with existing cardiac disease the hope for improvement placed in tonsillectomy has not been certain. If tonsillectomy is to be generally used in the future as a definite therapeutic measure in cardiac disease, its best result will be obtained before the incidence of heart infection or very early in its course.

The author points out that carditis is but one phase of a generalized infection spoken of as rheumatic fever. The tonsils may, or may not, be the existing focus which keeps up this infection. If the tonsillectomy is accomplished after the onset of carditis it will not necessarily prevent further recurrences because the cause of the infection may still be present in the throat or elsewhere in the body. The preventive treatment should be based on the raising of the individual's resistance to infection by all possible means.

Freund, Ernst: Rheumatic Nodules in Chronic Polyarthritis. Wien. Arch. f. Klin. Med., 1928, xxvi, 73.

Discussing the clinical and anatomical appearance of rheumatic nodules in acute rheumatic fever and primary chronic arthritis with their numerous analogies the author feels that we are not able to determine the etiology of both diseases.

The anatomical and bacteriological study of six cases of chronic arthritis showed certain analogies anatomically with the subcutaneous nodules of rheumatic fever but the author was unable to isolate any organisms.

His findings are therefore inconclusive in determining whether both diseases have a similar etiology.

Bourne, Geoffrey: Notes on a Case of Heart Block Whose Grade was Decreased by an Inspiratory Increase in Sympathetic Tone. St. Barts. Hosp. Reports, 1928, lxi, 146.

The author reports a case of 2:1 heart block occurring in a woman with exophthalmic goitre. On observation, it was noted that an inspiratory decrease in the block occurred and that for a few beats a 1:1 rhythm was present.

To discover whether this phenomenon was due to vagal inhibition, sympathetic stimulation or the result of increased heart filling various tests were tried.

The influence of the vagus was investigated by giving atropine and pilocarpine. With the former drug the respiratory reflex was more pronounced, with the latter, it was abolished; but no decrease in the amount of the block was observed. Ocular and vagal pressure was ineffective. The effect of stimulation of the sympathetic was investigated by noting the effect of adrenalin, exercise and psychical excitement. It was found that adrenalin temporarily abolished the block and that emotion seemed to have a similar transient effect. Exercise did not change the inspiratory block-decreasing effect. No effect on the degree of block was obtained when the heart was overfilled by pressure on the patient's abdomen. The respiratory reflex remained.

The author concludes that the respiratory effect is due to an increase in the sympathetic tone occurring during inspiration.

Bourne, Geoffrey: The Treatment of Rheumatic Carditis. The Lancet, August 4, 1928, 217.

The author summarizes the physical signs of active cardiac infection in rheumatic children. He emphasizes the need for prolonged bed rest, in such cases. The tonsils if diseased are removed. The criteria of tonsillar disease include the history of s

throats, the presence of cervical lymphadenitis and the appearance of the tonsils themselves. The dangers of tonsillectomy during the active stages of the disease are stressed.

Salicylates by mouth and a gargle of potassium permanganate are recommended. No encouraging results have been obtained from the use of vaccines, from intravenous disinfectants or from artificial sunlight.

Wiechowski, W.: Treatment of Cardiac Syncope. Wien. Klin. Wchnschr., 1928, xli, 475.

The author discusses the different forms of cardiac syncope due to injury to the heart, peripheral circulation or nervous system. He reviews briefly the methods which have been employed to test the effect of drugs on the circulatory system. According to Wiechowski, the effect of drugs can best be judged from their effect on the minute volume. He and his coworkers have investigated the following substances: camphor, digitalis, caffein, adrenalin and three new drugs with an effect analogous to camphor: Kardiazol, Coramin and Hexeton. The results of this work have already been published. Caffeine and adrenalin alone are reliable in producing an increase in the normal minute volume of the heart. In agreement with the findings of Winterberg and American investigators camphor has very little direct effect on the heart and the vasomotor center, while the three drugs mentioned above stimulate the vasomotor center. Indirectly, camphor excreted in the lungs may produce here a dilatation of the vessels and the bronchioles and may thus have an indirect action on the heart.

For the practitioner caffein should be the drug used in all kinds of circulatory collapse both for its direct effect on the minute volume and for its dilatation of the peripheral vessels. After the heart has stopped beating, intracardial injection of caffeine is indicated. The use of adrenalin is limited because it forces a weakened heart to work against a peripheral vaso-constriction and increased blood pressure.

Musser, J. H.: Theophylline-Ethylenediamine in Heart Disease Associated with Pain. Jour. Am. Med. Assn., 1928, xci, 1242.

The abstracted histories of 20 patients with several types of heart pain are indicative of the therapeutic effect of theophylline-ethylenediamine. The greatest value of the drug lies in the treatment of patients with angina pectoris. It is only slightly less valuable in the handling of patients who have survived the initial effect of coronary thrombosis.

The author points out that rest in bed, diet and proper fluid intake alone will be sufficient in many cardiac patients to restore compensation. However, it definitely seems that patients with comparable signs and symptoms of cardiac failure of a congested type improve more rapidly and more fully with digitalis therapy combined with rest in bed and theophylline-ethylenediamine than they do under the same regimen without theophylline-ethylenediamine.

Smith, Fred M.: The Diet and Theophylline in the Treatment of Cardiac Failure. Jour. Am. Med. Assn., 1928, xci, 1274.

Further observations on the diet previously reported have emphasized the importance of this feature in the treatment of cardiac failure.

A greater significance is attributed to the carbohydrates and particularly the sugars of the diet. The beneficial action of carbohydrates on the liver injury induced by prolonged congestive failure may contribute to the effectiveness of the diet.

Intravenous administration of dextrose solution is not advocated if the patient is able to take food by mouth. It is felt that the diet is a more effective means of providing sugar.

Theophylline is a valuable measure in the treatment of the cardiac failure of arteriosclerosis. The best results are obtained in the congestive type of failure. Experimental and clinical observations support the belief that the elimination of fluid is promoted by the favorable influence on the coronary circulation.

Lukens, F. D. W.: **Tolysin in Subacute Rheumatic Carditis.** Jour. Clin. Invest., 1928, vi, 319.

In order to determine the effect of tolysin on subacute rheumatic carditis, the author selected 6 children with rheumatic heart disease in whom the joint symptoms were minimal and the carditis the most prominent feature. The diagnosis in all these cases was rheumatic heart disease, active, with mitral stenosis and insufficiency and enlargement of the heart. There were no arrhythmias and although the lesions were fairly severe, none of these patients showed failure of compensation. The pulse rate was not affected by treatment in any of these patients.

The absence of any demonstrable effect of tolysin upon the weight, temperature and leucocytosis in this type of rheumatic heart disease is evident from the data published in the tables.

Graham, Stanley: **Arsenic in the Treatment of Chorea.** Arch. Dis. Childhood. 1928, iii, 206.

The author surveys the results of 3 forms of therapy used in 3 groups of children suffering from chorea. One group was treated with intravenous neokharsivan an average of 0.465 gm. arsenic being given per patient during thirty days. A second group was given liquor arsenicalis (liquor potassii arsenitis), the average amount of arsenic given being 0.276 gm. or about half the amount administered to the first group. A third series was treated with sodium salicylate.

The series of patients was further subdivided according to the length of time chorea had been present before treatment. The duration of the chorea in days subsequent to treatment and the condition of the heart on admission and discharge was taken as the criteria of the efficacy of the drug.

As far as the duration of the disease was concerned, the group treated with salicylates improved the quickest, and those treated with intravenous arsenic most slowly.

The heart murmurs cleared more in the group treated with Fowler's solution than in the other two.

The author concludes that drug therapy is of little value in chorea, that improvement is due to the tonic effect of the arsenic and is not proportional to the amount given. General measures are recommended and the use of sodium salicylate for its action on rheumatic manifestations.

Turner, Roy H.: **A Sphygmograph Using a Carbon Grain Microphone and the String Galvanometer.** Bull. Johns Hopkins Hosp., 1928, xliii, 1.

A sphygmograph for clinical and experimental purposes using the string galvanometer as a recording instrument is described and its possibilities indicated.

A carbon grain microphone mounted over the vessel through variation in pressure causes the current passing through to pulsate. These current pulsations are recorded by photographing the shadow of the galvanometer string.

The microphone functions largely as a result of pressure changes rather than movement of parts. The instrument is without demonstrable lag.

Records show a form agreeing with accepted standards, and exhibit accuracy of the time element.

Turner, Roy H.: A Method for Measuring the Velocity of the Pulse Wave in which Helium Glow Lamps are Used as Markers. Bull. Johns Hopkins Hosp., 1928, xliii, 14.

An instrument and method for measuring the velocity of the pulse wave is described. The flashes of helium-filled glow lamps photographed on the moving film serve to indicate the time of arrival of the pulse under carbon grain microphones.

The instrument is without demonstrable lag.

The beginning of the flash may be made to coincide with the beginning of the upstroke of the sphygmogram.

Detailed data for determination of pulse wave velocity in six subjects are presented.

Marvin, H. M.: The Heart During Anesthesia and Operative Procedures. New Eng. Jour. Med., 1928, cxcix, 547.

The author discusses this important subject from the standpoint of general anesthesia procedure by ether, ethylene and nitrous oxide gas. He presupposes that chloroform produces definite injury to the heart and that in the hands of inexperienced anesthetists any anesthetic may injure the patient at this time.

He believes there is no convincing evidence that anesthesia and operation in themselves have any damaging action upon the normal heart. The damaged heart whatever its physical signs is the equivalent of a normal one for anesthesia and operation if it is carrying on an adequate circulation under normal conditions of life with a possible exception of the syphilitic heart; no matter what size the heart may be, no matter what thrills or murmurs may be present over the precordium, no matter how far nor in what direction sounds or murmurs may be transmitted if the patient has been leading the life involving moderate activity and has been without symptoms it may be safely assumed that it will behave properly during anesthesia and operation. There are three types of heart disease that are notoriously apt to lead to sudden death, even at complete rest: syphilitic heart disease with aortic insufficiency, complete heart block as a manifestation of any type of heart disease and that form of heart failure known as angina pectoris. The history, therefore is more important than the physical examination although both should be obtained.

Patients with heart failure and those of auricular fibrillation even without heart failure should receive digitalis before operation if possible. The digitalis should be given in therapeutic doses or not at all and it should not be given as a routine preoperative measure.

Of the available general anesthetics, ethylene gas is probably the one that has the most to commend it, for use in patients with heart failure; and finally possibly most important of all it is more important to select the proper anesthetist than to select the anesthetic.

Book Reviews

Harvey, William: EXERCITATIO ANATOMICA DE MOTU CORDIS ET SANGUINIS IN ANIMALIBUS, With an English Translation and Annotations by Chauncey D. Leake. Charles C. Thomas, Publisher, Springfield, Illinois, 1928.

This book is published as a tercentennial edition of the original book by Harvey. Part I consists of a facsimile of the Latin edition reproduced by a new and exceedingly accurate process in photo-engraving. Part II is the English translation made by the author. This translation is based on the Longhine edition of 1697. Willis' translation of the dedication has been included since this is missing from the Longhine edition. The translator has also made use of a copy of Moreton's privately printed facsimile of the original edition. From these two sources, the author has prepared his own translation. He states that he has made this admittedly free in a deliberate attempt to present Harvey's thoughts in the current physiological manner. Thus while Harvey nowhere uses a word which may be literally rendered "pump" the author prefers to refer to cardiac action in some such term.

In order to bring out the significance of Harvey's work in regard to our modern knowledge of cardiac function, and to relate it to the slow development of this knowledge footnotes have been added to the translation.

This volume in connection with others which have appeared this year as part of the tercentennial celebration of the appearance of Harvey's great book should appeal strongly to students of Physiology and also to those interested in Medical history. A chronology of the life of William Harvey has been added.

There are included 10 illustrations, chiefly reproductions of the well-known Harverian pictures. These have been carefully collected from well-known sources and are presented in this volume in excellent form. They add greatly to the value of the book.

The book was set, printed and bound by the Collegiate Press, Menasha, Wisconsin. The cover design and front matter have been prepared and set with great care. The type face of the English translation is the very beautiful Caslon Old Style No. 337. It was designed by William Caslon, an engraver, in the early eighteenth century. Its characteristic is that of simple, honest design and perfect craftsmanship. The paper is eighty pound Natural Laid Aurelian Book.

The author has selected the material carefully and has rendered an excellent translation, avoiding all stilted and involved terms. The reading of this translation is easy and fascinating. It marks a distinct advance in publication of medical historical volumes.

The publishers are to be congratulated on the fineness of form and great attention to interesting and professional details.

CRITERIA FOR THE CLASSIFICATION AND DIAGNOSIS OF HEART DISEASE. By a Committee (Joseph H. Bainton, M.D., Robert L. Levy, M.D., W. C. Munly, M.D., M.C., U.S.A., and Harold E. B. Pardee, M.D., Chairman) Appointed by the Heart Committee of the New York Tuberculosis and Health Association, Inc., New York, Paul B. Hoeber, Inc., 1928, pp. 92.

The Heart Committee of the New York Tuberculosis and Health Association has devoted a great deal of attention to raising the standards of cardiac diagnosis, not only in the larger centers where the more elaborate methods of study are available, but in every Heart Clinic, no matter how small. The Committee believes that a complete and accurate diagnosis, including etiology, pathological anatomy, physiology and functional capacity, is of the greatest importance, and that a diagnosis made in one city should mean the same thing in any other city. In this little volume of 92 pages the Committee has brought together a commentary on the Nomenclature for Cardiac Diagnosis approved by the American Heart Association. This commentary takes up each heading, discussing it and defining the terms, and makes it possible for workers in all parts of the country to use the Nomenclature in a uniform manner. The discussion is practical and special emphasis is laid on methods of examination which are within the reach of everyone. With the aid of this book a complete cardiac diagnosis should be within the reach of every physician, and records from clinics in all parts of the country should be comparable for statistical studies in a manner not possible heretofore. The section on Etiology offers many valuable suggestions, perhaps the most valuable being the emphasis on the point that the correct etiological diagnosis is often "unknown." The sections on Anatomy, Physiology and Functional Capacity should be of general interest. There are suggestions for making an examination and a table of terms to be used in describing heart sounds and murmurs. Adherence to these systematic methods of examining and describing would result in reliable and easily interpreted records. Functional capacity is tested by the patient's ability to perform physical activity, not by arbitrary tests, and it is important to note that the functional classification depends solely on this ability and is not to be influenced by the anatomical prognosis or the prognosis. The term "Fibrosis of the Myocardium" is added to the headings.

A few points raise a question in the mind of the reader. The relation of hypertension to arteriosclerosis seems dogmatic; the diagnosis of tumor of the heart and of adherent pericardium seems almost too easy; and the discussion of "potential" and "possible" heart disease is rather brief. On the whole the style is as clear as it is concise, and the criteria are those which can be determined and used by all workers. There is now no excuse for incomplete or inaccurate records.

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Original Communications

ECONOMIC ASPECTS OF HEART DISEASE*

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No small part of the present colossal wealth of our country is due to the accumulated saving of the lives of men and women in the years of their greatest material productivity, by the fall in the death rate from pulmonary tuberculosis. It is unlikely that in this country and in our time any other change in the prevalence of disease can produce such impressive increase in the earnings and savings of our people. Now that tuberculosis has lost its leadership of the column of deaths and heart diseases have emerged, partly by the fall in the death rates from other causes and partly because of the great and sustained increase in the death rates from heart disorders as the most frequent of the causes of death, popular interest, as well as medical, drives us to analyze causes and costs in this field of pathology as a community problem.

In 1921 it was estimated that the *per capita* cost of tuberculosis to the people of the United States was \$7.96 annually, and that this burden, if distributed among those persons with an active, clinically recognizable tuberculosis, amounted to \$1,262 annually per patient, and that the total loss due to tuberculosis during the entire life span of the population at the then rate of tuberculosis mortality would amount to \$27,125,000,000.[1]

No better confirmation of the adage, "The first wealth is health," is to be found than the estimate of economists that the value of human lives in this country is at least five times that of all material possessions.[2]

While the implications of the title of this paper may be as broad as the range of human activities, it will be understood for present purposes that "economics, or political economy, is the social science which treats of that portion of human activity which is concerned with earning a living," and that under the term heart disease are included those various conditions provided for under the four titles

*Presented before the Congress of American Physicians at Washington, D. C., May 2, 1928.

of the International List of Causes of Death, 87-90—Pericarditis, Endo- and Myocarditis (acute), Angina Pectoris, and Other Diseases of the Heart.

We are necessarily limited to the use of these few terms, inadequate as they are, because with rare exceptions under no others are there to be found records of the distribution and duration of heart diseases which permit us to estimate the character and the extent of the influence of this particular group of disabilities upon earning capacity and span of life.

The bearing of disease upon the earning of a livelihood depends at least upon the age of the person at onset, the degree and duration of disability as the process develops, and the extent to which death from this cause shortens life.

Information is therefore to be sought from the records of deaths, and of sickness, where these latter are assembled through institutions or agencies, such as hospitals, dispensaries, visiting nurse associations, industrial and insurance or compensation offices.

While no economist or statistician can express in figures alone the value of man's life, there is a trustworthy method of calculating in terms of earnings, the relative returns on the investment of life when death comes to man at different ages.

The studies of Dublin and Lotka[2] will be used as the basis of estimating the economic losses due to heart disease in this paper. By these authors the money value of a life at a given age is considered to be the difference between the person's calculated future earnings at the time of his death, and the present worth of his probable future expenditures.

Since the overwhelming majority of men in the United States today are found in, or at least nearer the $2,500 income class of earnings than in the $5,000 a year class or over, we shall confine our estimates to the former without attempting to make allowance for that relatively very small proportion of heart patients and deaths occurring in the higher income group. For convenience of reference, however, the accompanying abbreviated table from the studies of Dublin and Lotka will indicate the relative values of these two groups of earners expressed in dollars of value at the age of death.

ESTIMATED VALUE OF A MAN'S LIFE IN TERMS OF NET FUTURE EARNINGS AT VARIOUS AGES

Year of Age	*On Basis of $5,000 Annual Earnings*	*On Basis of $2,500 Annual Earnings*
18	$34,321	$28,654
21	39,176	30,818
30	48,562	31,038
40	45,670	25,795
50	30,354	17,510
60	10,256	8,499
70	5,988	562

Our knowledge of the degree of disability due to heart diseases during the various phases of their preclinical and recognized existence in man is too fragmentary to justify us in attempting calculations in this field. For persons completing the years of their normal life existence; i.e., with undiminished average length of life, though handicapped because of limitations in physical vigor, skill, or endurance because of disease, reliable estimates of money value at the various ages can be made as has been indicated by Dublin in his table on Substandard Wage Earners in Three Income Classes ($500, $1000, and $1500).[3]

The burden of heart diseases caused by the shortening of the life of occupied and retired civilians, from twenty to sixty-five years of age,[4] is heavier among the unskilled workers than in any other social class, the unskilled workers' comparative mortality figure from this cause being 156.5, while that of the upper and middle class is 105.8 and that of skilled workers is 120.1, a difference to the disadvantage of the low income level group which is found also in tuberculosis, cancer, and pneumonia.

This difference is particularly marked when the death rates from heart diseases by social classes are analyzed by age groups, the unskilled workers suffering out of proportion in all decades of life, but particularly in those under sixty-five years, as shown in the accompanying list.

Age	*Unskilled Workers*	*Skilled Workers*	*Upper and Middle Class Workers*
16 - 19	25	18	6
20 - 24	34	25	15
25 - 34	55	37	18
35 - 44	91	61	43
45 - 54	181	127	112
55 - 64	454	394	401
65 - 69	946	907	977

As the Registrar General remarks, "It is evident that in early and middle life at least, heart disease as a whole is found to be especially fatal to the poorer classes, and although no record has been obtained of the social incidence of mortality from acute rheumatism, it is to be presumed that even if all classes were equally subjectable to this disease its effects upon the valves of the heart would be more serious to those least in a position to take the necessary precautions."

When the mortality from valvular disease of the heart is distributed by specific occupations, the death rates from this condition are found to vary widely according to the character of employment.

If we consider the death rate from valvular heart disease of all occupied and retired males (twenty to sixty-five years) as 1,000 we find the low mortality rates among,

Insurance officials	230
Gamekeepers	249
Bank officials	334
Anglican clergy	391
Millers	393
Medical practitioners	438
Roman Catholic priests	472

Those occupations with a high ratio of mortality from this cause are:

Cotton carders	2170
Cotton strippers and grinders	2063
Barmen	2024
Slate masons	1994
File cutters	1852
Cutlery grinders	1727
Slaters and tilers	1727
Cotton blowroom operatives	1688
Wool weavers	1666
Slate miners	1647

Similarly the occupations showing particularly high mortality rates from "Other heart diseases" (chiefly myocardial) include many low paid and disadvantageous employments.

Tin and copper miners below ground	3244
Cutlery grinders	2834
Slate masons	2642
Barristers	2514
Hat formers and plankers	2317
Tin and copper miners	2242
China, kiln, and ovenmen	2122
Pottery dippers, glazers, etc.	2108
Cellarmen	2029
Cotton carders	1869

From the less ample and conclusive evidence in this country we find, as given in Pedley's[5] tables of proportionate mortality from principal diseases among ten occupations in New York City, 1924, that butchers, tailors, cigar makers, and shoemakers have death rates from heart diseases considerably higher than the rate for all the occupations listed as a group. Furthermore, it is seen from this same study that in 1920 the proportionate mortality for occupied males in the United States, ten years and over, was higher from heart diseases than from any of the other six leading causes of death.

The duration of heart disease as determined by various sickness surveys, reported by Frankel and Dublin (1915-17) in North Carolina, Pennsylvania, New York,[6] and Massachusetts differs radically from the duration of all sicknesses taken as a group. Calculations based on these surveys justify the following statements:

One-quarter of all sicknesses lasting less than two weeks; 3.7 per cent of all heart disease lasting less than two weeks.

Fifty-four and eight-tenths per cent of all sicknesses lasting less than three months; 28.6 per cent of heart disease lasting less than three months.

Seventy per cent of all sicknesses lasting less than one year; 50.5 per cent of heart disease lasting less than one year.

Sixteen and eight-tenths per cent of all sicknesses lasting three years and over; 24.2 per cent of heart diseases lasting three years and over.

Among New York State factory workers in 1919,[7] 1.2 per cent of total wages were lost on account of heart diseases, or $66.11 lost per case, while 2.2 per cent were lost on account of tuberculosis, $230.51 lost per case.

Sickness from organic heart disease among office employees in a large commercial office[8] in New York City caused a loss of two hundred fifty-three and nine-tenths working days per annum per 1000 persons employed, and showed a loss of ninety and six-tenths days per case of illness which constituted 2.68 per cent of all working days lost, the differences between male and female workers being of no significance. There were lost on account of heart diseases 296.8 calendar days for each 1000 persons employed, or 105.8 calendar days per case of heart disease, or 2.78 per cent of all calendar days lost on account of sickness among these employees. There were 2.8 cases of heart disease per 1000 persons employed in 1925 amounting to 3.4 cases per 1000 clerk years or 0.13 per cent of all cases of disability for that year.[8]

Analysis of health insurance claims on account of heart diseases[9] shows that ninety and four-tenths days are lost per claim, varying according to the age of the claimant from forty-two days among those twenty-five to twenty-nine years of age to one hundred twenty-three and one hundred fifty days among those fifty to fifty-four and fifty-five to sixty years of age respectively.

In Brundage's study of *Sickness Among Industrial Employees*[10] he found that according to the length of the maximum disability period provided for, the number of days of disability per case varied from sixty-five to one hundred twenty-two days, as compared with the duration of disability per case of eighty-four to one hundred sixty-one days in tuberculosis.

In the same report the average annual number of cases of heart disease as a cause of sickness disability per 1000 male industrial workers (1922-24) was found to vary from 1.1 in the public utilities to 1.4 among the iron and steel workers, and 1.5 in other industries.

In Dublin's study of *Causes of Death by Occupation* from the Metropolitan Life Insurance Company mortality experience,[11] deaths from organic heart disease constituted 12 per cent of deaths from all causes varying from 5.4 per cent among railway enginemen and trainmen to 16.5 per cent among farmers and farm laborers and for females 14.8 per cent, ranging from 8.1 per cent among bookkeepers and office assistants to 15.3 per cent among housewives and housekeepers. These differences are doubtless due in large measure to the small number of cases dealt with as well as to the age groups of the persons involved.

A further analysis of Dublin's study reveals for all occupations the percentages of all deaths represented by those due to heart diseases, according to the sex and decade of life of the deceased as shown in the accompanying age groups:

AGE GROUPS

	15-24	*25-34*	*35-44*	*45-54*	*55-64*	*65* AND OVER
Males	5.8%	5.4%	7.7%	11.1%	15.9%	20.4%
Females	6.9%	7.0%	10.0%	13.9%	18.7%	20.8%

Similar information upon percentage of all deaths represented by deaths from heart disease and decade of death is found in Wynne and Guilfoy's[12] report for experience among employed males in New York City, 1914, as here shown.

AGE GROUPS

15-24	*25-34*	*35-44*	*45-54*	*55-64*	*65* AND OVER
8.4%	8.7%	10.3%	17.6%	22.2%	28.0%

In both these reports there are considerable differences according to sex and occupation, but the variations are quite consistent among the age groups.

Regardless of age and sex, the variations in the percentage which heart disease deaths constitute of all deaths, by occupations, were found by Wynne and Guilfoy to be as follows:

	Per Cent
All occupied persons (53,541)	17.9
Blacksmiths	15.8
Cigar makers and tobacco workers	18.9
Clerks and bookkeepers	14.0
Compositors and printers	13.6
Garment workers	20.7
Laborers	13.4
Machinists	14.1
Painters and paper hangers	14.9
Railroad track and yard workers	17.6
Saloonkeepers and bartenders	10.1
Teamsters and drivers	10.3

In Brundage's study of a ten-year experience with absences from work in the Edison Illuminating Company of Boston he found that there were for both men and women, 4 absences for heart diseases among each 1000 on the payroll per annum, but that while the men lost forty-nine and fifty-two hundredths calendar days on account of each such sickness, the women lost ninety-nine and seventy-three hundredths days.

Of the total deaths from all causes in the United States Registration Area, 1925, 1,219,019, there were 191,226, or 15.7 per cent, from heart diseases. Of these (215 age unknown), 170,482, or 89.2 per cent, were in persons forty years of age or over.

40 - 49 years of age	16,384
50 - 59	28,118
60 - 69	44,843
70 - 79	49,774
80 - 89	27,262
90 and over	3,886
Unknown	215

There were only 20,744 deaths from heart diseases in persons under forty years of age.

Under 10 years of age	3133
10 - 19	4095
20 - 29	4879
30 - 39	8637
	20,744

The decade seventy to seventy-nine years in which the largest number of deaths occurred is the last one for which Dublin estimates that there is any balance of money value in favor of the individual between his probable earnings and expenditures.

The largest number of deaths from nephritis and from cerebral hemorrhage also occur in the decade of life seventy to seventy-nine years, while the largest number of deaths from cancer occur in the decade sixty to sixty-nine and of tuberculosis in the decade twenty to twenty-nine years.

Not alone the total number of deaths from a particular disease, but their distribution among the decades of life, and the duration of the disease as a cause of relative or complete disability are the determining factors of its economic cost to the individual and the community.

In dealing with heart disease we must consider duration and death, moreover, on the basis of the three dominant etiological groups, rheumatic, syphilitic, and arteriosclerotic or senescent.

In translating clinical histories into graphic form for the purpose of expressing the spread of disability and death across the years of life, we have the following pictures of the three groups mentioned. (See Fig. 1.)

When rheumatism completes its cycle from onset through a period of disabling symptoms to and through the time of decompensation to death, all under the age of forty, which occurs in the great majority of cases, we find that the onset is under ten years of age in 19 per cent of the cases, between ten and twenty years of age in 37 per cent, between twenty and thirty in 23 per cent, and between thirty and forty in 21 per cent of the cases. Furthermore, we find on the average, a duration of four years between onset and partially disabling symptoms, which thereafter continue about seven years before decompensation, and with it probably complete disability develops, which continues, alternating with partial and occasional working ability, for four years until death.

With syphilis, the infection which occurs between eighteen and thirty years of age is followed, so far as heart disease including aortitis is concerned, by from ten to twenty-five years without symptoms or conscious disability, death following usually within two years after the development of disabling symptoms. The deaths from syphilitic heart disease are therefore to be found in 80 per cent of the cases after the age of forty, in 12 per cent in persons over sixty, and in about 34 per cent of the cases each in the decades forty to forty-nine and fifty to fifty-nine years.

Of the 20 per cent of syphilitic cardiac deaths occurring under forty years of age, 3 out of 4 are in the decade between thirty and forty years.

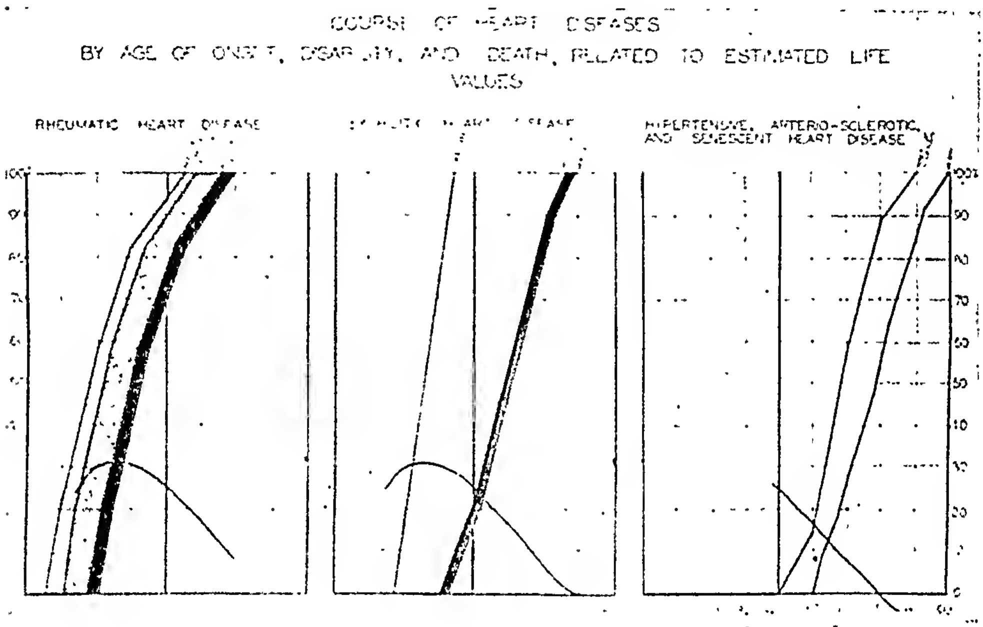

Fig. 1.—In this figure will be found graphically expressed the life history of the average heart patient of each of the three chief categories of heart disease across the span of life (summarized from the literature by Cohen[13]).

The onset of rheumatic heart disease occurs in 60 per cent of the cases before the age of twenty years and in 95 per cent before the age of forty. The period of time between infection and the development of disabling symptoms is usually longer in those attacked early in life than in those attacked after twenty, as shown by the varying width of the lightly shaded strip averaging a little less than four years in duration.

Following this is a fairly uniform period of seven years (heavily shaded strip) during which there are disabling symptoms of varying severity but causing interference to marked degree, though intermittently with usual occupations.

Finally, the solid black strip expresses the period of about four years of increasing and almost continuously complete disability until death results from cardiac failure.

The curved line *A* represents the changing value of a life expressed in dollars, throughout the period of prevalence of rheumatic heart disease as indicated at the right hand of the graph.

The same use of lines and spaces prevails in the graphs of experience with syphilitic and hypertensive or senescent heart disease.

In the great mass of all deaths attributed to diseases of the heart, those of the senescent type, constituting 90 per cent of the total, the onset of symptoms occurs (according to Wyckoff[14]) by decades as here shown:

Age	*Per Cent*
30 – 39	0.4
40 – 49	14.1
50 – 59	43.6
60 – 69	31.6
70 and over	10.2

This type of heart disease is not accompanied by any more, or other disability than is commonly found among all persons in the later decades of life, the subjective symptoms of the disease rarely causing the patient serious occupational handicap unless he be alarmed by what he is told about his sickness.

In most cases in the senescent type of the disease, cardiac failure of a disabling degree occurs, if at all, so near to the time of death and at so late an age that a calculable period of economic disability does not develop.

Practically all deaths attributed to the senescent type of heart disease occur after the age of fifty, their distribution among the subsequent decades of life being as shown in the accompanying table.

PERCENTAGE OF ALL DEATHS FROM SENESCENT HEART DISEASE FALLING IN THE DECADES

Years	*Per Cent*
50 – 59	18
60 – 69	29
70 – 79	33
80 and over	20
	100

The following are typical composite histories from patients among the low income or dependent class, representing the three groups of heart disease leading to death, as assembled from the use of the detailed record forms, issued by the New York Heart Association.

Rheumatic Heart Disease.—White male patient, born in the United States of Italian parents. Reported at clinic at age of sixteen years. Patient had had rheumatic fever at the age of eleven and again at fourteen. At the age of fourteen he began to have symptoms referable to his heart, dyspnea, and precordial pain. A tonsillectomy was performed at the age of fifteen. When patient was seen in the clinic at age of sixteen, the diagnosis of mitral insufficiency and stenosis was made. At the age of eighteen he had his first attack of cardiac failure, with symptoms of dyspnea, orthopnea, and precordial pain. He was cyanotic and his liver was palpable. The following year, at the age of nineteen, he had another attack of failure, more severe than the first. The patient died at the age of twenty-one of progressive congestive heart failure.

Syphilitic Heart Disease.—Male patient was admitted to the clinic at the age of forty-nine years. He had had gonorrhea at the age of twenty-three and syphilis at the age of twenty-four. At the age of forty-eight he began to have cardiac symptoms, which progressed markedly until he died at the age of fifty.

Arteriosclerotic Heart Disease.—Male patient was admitted to the clinic at the age of fifty-five years. At the age of forty-nine he began to have symptoms of heart failure but not of a degree of severity to interfere with work. The disabilities progressed until the time of his death, at the age of fifty-seven.

Estimates of the cost of heart disease in the United States can be approximated by calculating the losses due to premature deaths, and the costs of medical and nursing care, as in hospitals, dispensaries, by visiting nurses, in convalescent homes, and in homes and hospitals for chronic invalids.

Death Costs, 1928.—The population of the United States is estimated as of July 1, 1928, to be a little over 120,000,000. The death rate from heart diseases (87-90) in the Registration Area in 1925 was 185.46 per 100,000 of the population.* It is estimated that the deaths from heart diseases in 1928, if the rate of 1925 is not exceeded, will be 221,809. When distributed by age groups according to the distribution in per cent of heart deaths in 1925 and charging for the numbers occurring at each decade, the value of a life at the mid-period of the decade, we find the loss in terms of money value to be \$1,538,897,680, or \$12.65 per capita of the population.

Age Group	*Estimated Distribution of Deaths From Heart Disease 1928*		*Life Value at Mid-period Age*		*Loss to the Community*
	Per Cent	*No.*			
Under 10 yr.	1.6384	3,561	\$14,156		\$ 51,598,620
10 – 19	2.1414	4,673	25,341		120,724,524
20 – 29	2.5514	5,564	31,900		181,061,400
30 – 39	4.5166	10,015	28,750		288,851,250
40 – 49	8.5679	18,917	22,000		419,298,000
50 – 59	14.7041	32,493	12,900		421,946,100
60 – 69	23.4503	52,200	4,400		229,530,400
					\$1,713,013,294
70 – 74	13.4982	30,027	– 766	\$ 23,000,682	
75 and over	28.9317	64,359	– 2,348	151,114,932	
					– 174,115,614
	100.000	221,809			\$1,538,897,680

While it may be quite justified from a purely financial point of view to calculate the loss to the community of the life of a woman on the basis of 50 per cent less monetary value than that of a man at the same age, there is a good reason to consider that the loss of life from heart diseases among women, decade by decade, and for equal numbers, constitutes quite as heavy a financial loss to the family and home in terms of dollars' worth of service and care, as results from the same cause in the male. This is particularly the case in the economic group we are using as the basis of our estimates; i.e., persons earning \$2,500 a year or less. Therefore, no attempt will be made to proportion the total cost of heart disease, sickness, and deaths according to sex incidence.

*This death rate was 199.1 in 1926 and in all probability the rate for 1928 will be well over 200, but since the other data to be referred to is most of it available for periods not later than 1925, the calculations can more conservatively be based on the 1925 death rate of 185.46.

The death rate from heart disease in the registration area[15] having increased 27.3 per cent from 1920 to 1925 (31 per cent among males, 18 per cent among females), it is certain that the 1928 estimate of deaths from this cause is conservative and well within the truth.

Hospital Costs.—In 1927 in the 4322 general hospitals in the United States, 66 per cent of the 345,364 beds were used on the average throughout the year, or 227,940. It was found[16] in 1921, in New York City, that while 4.6 per cent of all general hospital patients are admitted for heart disease, 9.1 per cent of the days of care provided in these hospitals are for this class of patients, or a total of 7,562,837 days of care for heart patients in the United States or, at an average cost of $4.00 a day per patient, a cost of $30,251,348. The average cost of hospital care in public general hospitals in New York State has in recent years (1926) been $3.08 per patient day, and in private or so-called endowed general hospitals $4.90 per patient day.

The experience of the State of New York including the City of New York shows a much smaller proportion of all hospital patients to be heart patients (1926[17]); i.e., 2.7 per cent in the general hospitals of the State and City as compared with 4.6 per cent in general hospitals in the city taken separately. If then the 2.7 per cent of all general hospital patients in New York State and City are heart patients, and we have learned (1926) that the heart patient on the average uses about 1.74 times as many days of hospital care as other patients do, we shall find when applying this situation to the hospitals of the country as a whole that there would be 4.698 per cent of total bed days of hospital use devoted to care of heart patients, or 3,904,319 days ($2.7 \times 1.74 \times 227{,}940 \times 365$) which at four dollars a day of care would be $15,617,276. The actual cost of hospital care for heart patients for the United States as a whole probably falls between these two figures; i.e., not over thirty nor under fifteen million dollars a year.

The reader familiar with the social practice of different parts of the United States as it affects the supply, use and *per diem* cost of hospital bed care for heart and other general medical patients will realize that estimates based on the experience in New York City and State may be in error, but information on the points at issue are not available from other large population groups. Also the fact that the reported death rate from heart diseases for New York State is higher than for any other state may result in an extent of hospitalization of this group of diseases above the average for the country as a whole. When more complete information is available, the estimates offered here and now will have to be revised, but if present trends in death rates and hospital use and costs continue, the revision is likely to be upward rather than down.

It was found, furthermore, that 7.4 per cent of the total cost of operating the public general hospitals in New York State, including New

York City, in 1926 went for the care of heart patients, and 3.6 per cent of the cost in the private general hospitals went for this purpose, the latter not being provided so commonly with beds available for the more chronic forms of disease. In the private hospitals in New York City the comparable figure was 4.3 per cent.

Nursing Visit Costs.—Approximately 3,000,000 persons are in the boroughs of Manhattan, Bronx, and Richmond of New York City, within the reach of the Visiting Nurse Service (The Henry Street Nurses). Among these people 304,367 nursing visits were made to patients discharged from care in 1927, of which 7,229, or 2.4 per cent, were for heart patients. Stated in another way these nurses visited 44,216 different patients in the year, of whom 692, or 1.6 per cent, were heart patients, who received an average of 10.45 nursing visits each.

Among the entire population of the United States, approximately forty times the size of the community served by these visiting nurses, either visiting nurses or other persons with less skill and at more expense directly or indirectly, will be found to be providing some degree of home nursing, or a total of 289,160 individual services, which at the present actual average cost of visiting nurse service of $1.00 a visit, would be $289,160.

Cost of Clinic Care.—The six million people of New York City appear to be adequately served by the several heart clinics, as far as heart patients, suitable on economical and pathological basis for ambulatory clinic care, are concerned. Almost all ambulatory heart patients not under the care of private physicians go direct or by reference from other out-patient or dispensary classes to the special heart clinics scattered throughout the city.

The patients attending these heart clinics numbered 10,017 (4592 adults, 5425 children) and made 37,871 separate visits.[18] Of the total number of patients 22 adults and 211 children were found not to be suffering from heart disease.

Thus we find that there was one heart patient attending a heart clinic in the year for each 600 persons in the population and one clinic visit was made in the interest of heart disease by these patients for each 150 persons in the population.

It is known that as many as one-fourth of the entire population of the city calls upon the dispensaries for medical care in a year. We may reasonably estimate that there are four times as many ambulatory heart patients in the city receiving some medical care (three-fourths of them presumably at their own expense) as there are patients attending heart clinics.

Applying this ratio we should find that one person in 150 of the population of the country is a heart patient (800,000) capable of visiting a physician's private office or a public clinic, and that there is

made one visit by these heart patients each year for each forty persons of the entire population.

At this ratio we should have about 3,000,000 visits a year, those at the public dispensaries costing the public and the patients about $1.00 a visit to provide, and the rest costing $2.00 or more for each visit, or approximately $750,000 for the dispensary visits and $4,450,000 for private physicians' care or $5,200,000 for the population of the country as a whole.

The possible error of too high estimates based on experience in New York City is recognized, but final correction on the basis of morbidity records on a national basis must wait for the distant future. It must be remembered that the American heart movement had its origin in New York City and the more the knowledge of prevalence of heart disease is developed elsewhere the nearer do other communities approach the records of New York.

Convalescent Care Costs.—We have estimated (on the basis of New York City's experience) that there may be 7,562,837 days of hospital care given to heart patients throughout the United States in a year, and about half as many if we base our calculations upon use of beds for heart patients in hospitals throughout the state outside of New York City.

In 1923 it was found[16] that in large general hospitals of New York City the average length of stay of heart patients was fifty-two and two-tenths days for each such patient admitted, the length of stay varying from twenty days at Bellevue Hospital to one hundred and forty days at the City Hospital for chronic invalids.

It was found in 1927[17] that the average length of stay of heart patients in 101 general hospitals in the state of New York was twenty-four days, varying from fourteen and three-tenths days in Westchester County to thirty-three days in Erie County, New York County giving twenty-six and three-tenths. Taking the more conservative and probably more representative figure of twenty-four days' care per patient, we can estimate on that basis that there were somewhere between 160,000 and 315,000 heart patients admitted to general hospitals according to our use of state or city figures for the number of beds occupied by heart patients in general hospitals.

It has been found in various surveys of hospital and dispensary practice and from studies of the needs of patients as discharged from hospitals[19] that among general medical and surgical patients and maternity patients about 10 per cent needed as much as three weeks' convalescent care. More nearly twice as many of hospital heart patients require such a convalescent period as do the general run of patients, and for a six weeks' period instead of three weeks.

Similarly it is found that, while of general dispensary patients some 2 per cent need convalescent care for three weeks, probably at least

4 per cent of heart patients attending clinics need such care for as much as six weeks.

Twenty per cent of hospital heart patients would be somewhere between 32,000 and 63,000 according to our basis of estimating heart patients as above. Four per cent of the probable one-fourth of the ambulatory heart patients attending clinics (200,000 as given above) would be 8,000. Six weeks' convalescent care for these two groups of patients would amount to somewhere between 1,680,000 and 2,982,000 days of convalescent care.

This type of care costs about half as much *per diem* as does general hospital care, so the expense of such care if provided would be between $3.360,000 and $5,964,000.

We do not know the number of days of care provided for heart patients in convalescent homes, but we do know[20] (Bryant, *Convalescence*, 1927, pp. 255-257) that there are about 12,000 beds devoted to convalescent care for part or all of the year outside of the vicinity of New York City and about 3,000 more in the New York City environs. Many of these beds are available for only a few months each summer. Others, though intended for use throughout the year, are not always occupied, and there is no reliable record of the number of bed days of convalescent care provided for heart patients.

However, since New York City's 6,000,000 people are pretty well served in respect to convalescent care for heart patients by the 370 beds in use for this purpose throughout the year and used to a high percentage of their capacity, we might expect twenty times as many beds to be needed for the country as a whole or 7,400 which falls between the figures given above, 1,680,000 days of care calling for 4602 beds and 2,980,000 days requiring 8164 beds. Our estimates of cost are then within reasonable limits.

It is fully recognized that no such amount of care for convalescent heart patients is at present provided for in institutions operated for this purpose. However, if heart patients do not have such care in institutions or its equivalent under individual conditions, they will suffer avoidable damage from lack of it. Therefore, this item is added to the total estimate as a proper charge.

Chronic Sick Costs.—In a survey of chronic sickness, recently completed in Boston,[21] it was found that one person among every 185 of the population was a chronic invalid and that 19.6 per cent of these were heart patients, of whom 30.7 per cent were persons under twenty years of age and 42.01 per cent were persons under forty years of age. All but 30 per cent of all chronic heart patients were found to need care throughout the year, and it was further found that this was generally provided at about one-half the cost per patient day of the cost of care in general hospitals.

On this basis applied to the United States as a whole, the estimated 89,122 chronic heart patients needing care the year round are probably costing in the neighborhood of $65,059,060.00 a year. (120,000,000 ÷ 185 × 19.5 per cent × 70 per cent = 89.122. 89.122 × 365 × $2.00 = $65,059,060.00.)

Assembling our variously estimated items of the cost of the medical and nursing care of heart patients in the United States in this year, we have in round numbers for those:

A. Under care in general hospitals	$15,617,000 to $ 30,251,000
B. Under care by nursing visits in homes	289,000
C. Attending clinics or physicians' offices	5,200,000
D. Under care in convalescence	3,360,000 to 5,964,000
E. Under care in chronic stage	65,059,000
Total cost for a year	$89,525,000 to $106,763,000

We might properly say that we have estimated the above costs on the basis of a total of 1,148,800 to 1,179,800 heart patients of the various categories in a current given year or just under 1 per cent of the population as follows:

A. Under care in general hospitals	160,000 to 315,000
B. Under care by nursing visits in homes	27,680
C. Attending clinics or physicians' offices	800,000
D. Under care in convalescence	232,000 to 263,000
E. Under care in chronic stage	89,120
	1,148,800 to 1,179,800

Estimates have ranged from 1 to 2 per cent of the population as constituting the total of heart patients.

Using 1 per cent of the population as being nearer our own estimate, built up from the various groups probably receiving care, and using the lower of our total cost figures ($89,525,000), we find that the average heart patient in the United States today probably carries an annual charge of $74.60 or we might properly say that heart disease puts a burden of about 75 cents on each person of the entire population each year.

The cost of heart disease deaths occurring in the various decades of life was found to be $1,538,897,680 each year, or a loss of $12.82 for each member of the population.

In 1922 at the then death rate from tuberculosis in the United States, it was estimated[1] that the shortening of life by this disease, which amounted at that time to a reduction of the average length of life of all the people of the country by two and five-tenths years each, would cost the entire population of the country at that time during their complete life span the sum of $27,125,000,000.

On the basis that in 1928 heart diseases will cause a reduction in the average length of life of people in the United States of one and sixty-six hundredths years for males and two years for females, the cost to

those now living in the United States from the shortening of lives by heart disease will amount to $21,960,000,000 during their life span.

While heart diseases cause more deaths than tuberculosis, the age of death for the latter is much earlier, hence the greater effect of tuberculosis deaths on the average length of life, and on the cost of tuberculosis to the population as a whole.

It has been estimated recently by Louis I. Dublin[22] that the loss each year, on the basis of 1927 experience, due to the shortening of life by cancer, amounts to about $680,000,000 which may be compared with the estimates for the population of 1928 on the basis of the 1925 heart disease death rate, as presented above, $1,502,198,355, the greater annual cost from heart disease deaths being due to their greater frequency in the population, even though the largest number of deaths from this cause in any one decade of life is in a later decade than is the case with cancer deaths.

It was estimated on the experience of 1922 in the United States that the annual cost of tuberculosis patients was probably about $3.15 per capita of the population. It has just been shown that for heart patients the entire population must bear a cost of 75 cents per capita per annum. This difference in the cost is probably due to at least two important factors: namely, the greater adequacy of provision for the medical and nursing supervision of tuberculosis as compared with those available for heart patients, and the added costs of sanitary supervision and isolation of many tuberculosis patients, of a kind not required for heart patients, except for those in certain stages of acute rheumatic fever and its recrudescences.

Probably some postponement in the age of death from heart diseases of rheumatic origin and possibly some reduction in the incidence of acute rheumatic fever might result from an expenditure per patient, or per capita of population, for heart disease more nearly equal to the sums found desirable for the prevention of tuberculosis and the treatment of the tuberculosis patient.

The burden of heart disease falls more heavily, absolutely in terms of incidence and deaths, and relatively in terms of loss of livelihood, upon the unskilled wage-earner, the under-privileged man and woman, than upon any of the higher earning or social levels of the community.

Because of its duration, heart disease, with the exception of tuberculosis, mental alienation, and certain forms of chronic arthritis, constitutes heavier burdens upon wage-earners than do other diseases, this burden increasing with each decade of life from twenty-five to sixty-five.

Grateful acknowledgment is here made for the valuable material collected and prepared for use in this paper by Miss Jessamine Whitney and Miss Beatrice A. Myers of the staff of the American Heart Association and by Miss Claire Lingg of the staff of the Heart Committee of the N. Y. Tuberculosis and Health Association.

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EXPERIMENTAL PERICARDITIS*†

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Introduction

IT IS a matter of common clinical experience to have unsuspected cases of chronic adhesive pericarditis come to light at autopsy. These are usually revealed without ever having been suspected, or, at least, without having been diagnosed or clinically proved during the life of the patient. In a pathologico-clinical study of all of the cases of pericarditis that came to autopsy in the Charity Hospital at New Orleans during a recent five-year period we[1] confirmed this general conception of the present state of our knowledge of the subject. We found that there were no pathognomonic signs of an adherent pericardium either with or without mediastinitis, but not infrequently one or more of the classical signs was present. The presence of any one of these signs, we concluded, should lead to a thorough clinical study to substantiate or disprove the suggested diagnosis.

Almost every physician has seen cases of unmistakable acute rheumatic or tuberculous pericarditis subside and heal without leaving a vestige of the previous process. Often not one of the classical signs is discoverable even on the closest, particularly directed scrutiny. Yet these patients may present clinically more or less persistent cardiac embarrassment, and at autopsy there may be revealed a complete or partial obliteration or synechia of the pericardial cavity, with or without mediastinitis. A carefully elicited history is usually of distinct importance. It is, however, all too frequently negative.

The multiplicity of infrequent and obscure physical signs of extrapericardial as well as intrapericardial adhesions is most confusing. The need is apparent for more reliable physical signs and graphic pathognomonic evidence for establishing the diagnosis of chronic adhesive pericarditis. No shadow of doubt as to the presence of pericardial adhesions should be permissible where any such heroic therapeutic measure as surgical intervention is contemplated. We know of at least one instance where a patient, apparently without adequate study and certainly on insufficient evidence, was put through an unnecessary pericardiotomy. At the operation a perfectly normal mediastinum and pericardial cavity were exposed. Such an error emphasizes the necessity for more absolute criteria than we have had in the

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past. The hope of finding further diagnostic data apparently lies only in the diligent prosecution of further extensive experimental and clinical studies.

THE PROBLEMS OF CHRONIC FIBROUS PERICARDIAL ADHESIONS

The effects upon the heart itself of the various types of chronic fibrous pericarditis, that is, the pathological myocardial response to the different grades and types of pericardial lesions and the extent of the functional impairment, are not definitely established. The factors that determine the myocardial response to chronic pericardial injury and the mechanism of the same are not yet known. In our pathological studies we have been struck with the variability in the degree of cardiac hypertrophy and the rarity with which atrophy of the heart was found. The reasons for these variations have intrigued us.[2] We have calculated comparative heartweight-bodyweight ratios in the cases of dogs with various types of pericardial and mediastinal adhesions. We have turned to account the standards and methods that have been used in previous cardiac hypertrophy studies in the dog.[3]

The common type of chronic mediastinopericarditis is generally considered to cause an undue strain on the heart, especially when there is parietal chest wall anchorage. The precordial framework of ribs is frequently removed so as to relieve the heart from the tugging against a fixed, firm resistance. We are prone to consider this as little more than a first stage operation since the important intrapericardial adhesions remain.

A complete synechia without extrapericardial adhesions, it is quite generally argued, is of no serious moment and does not interfere in any way with cardiac function. With this conception we are not in accord. The lubricative function of the pericardium is perhaps of little significance. The presence, however, of dense adhesions in the interventricular grooves, where there is the least cardiac movement, is of serious moment since the major blood vessels traverse these grooves. Contracting adhesions, by constricting the vessels, inevitably interfere to some degree with the circulation of the heart itself. The pericardium is always pathologically altered by any inflammatory process, and its restraining function becomes significantly less effective.

Delorme[4] in 1898 on the basis of one poorly selected case, argued that intrapericardial adhesions were a source of serious embarrassment to the heart, and he contended that separation of the parietal and visceral pericardium should be accomplished by open operation. His contentions, however, are usually discarded with the argument that the adhesions invariably reform. V. Schmieden[5] has in recent years successfully dissected off the adherent pericardium from the ventricles, in human cases with cardiac failure, because of the embarrassing effect on the cardiac movements. The Brauer[6] operation of cardiolysis,

which consists in the removal of the rigid points of fixation, has received much more attention. This operation relieves the embarrassed heart to some extent where external adhesions have been firm and short. Yet it is merely a palliative procedure and does not correct or remove the significant intrapericardial lesions. These latter, we believe, are more significant than they are generally considered to be.

THE EXPERIMENTAL STUDY

For the past three years we have been engaged in the production of experimental pericarditis and the study of the clinical and anatomical facts gathered from these experiments. We have operated upon 125 dogs, but because of many technical difficulties only about half of our experiments have yielded data of significance.

Methods.—Our routine program for each dog has been rather extensive. Control fluoroscopic studies and roentgenograms were made. Control electrocardiograms with the animal in each of the three standard positions, on the back, on the left and on the right side, used to determine the presence or absence and the degree of shifting of the electrical axis, were taken with the animal under barbital anesthesia. Pericardiotomy was then performed under complete general intratracheal ether anesthesia, exercising at all times rigorous surgical aseptic technic. Irritating inorganic or organic compounds were introduced into the pericardial sac to produce the pericarditis. The pericardium and pleura as well as the thoracic incision were carefully closed. Fluoroscopic examinations and roentgenograms were then made, and electrocardiograms in the three positions were taken at irregular intervals and always just before the re-operation or the sacrificing of the animal with chloroform.

The dog's body weight was recorded and the heart carefully removed after making notes of all external parietal and mediastinopericardial adhesions. The type and extent of the visceral or intrapericardial adhesions and the degree of obliteration of the pericardial cavity were noted. The major blood vessels were cut short; the heart was then washed free of blood, fixed, cleaned, and divided, at a later date, according to the standardized technic previously described.[3] The weights and ratios determined were compared with the established normals.[3]

THE RESULTS FROM THE EXPERIMENTS

Clinical Data.—The significant data obtained from the series of experimental animals will be reported upon here in a summarized form. The clinical, or physical, examination of the dogs yielded little information of diagnostic importance. No neck vein phenomena could be seen in any of the animals even on careful inspection. Retractions of the precordial area were very infrequent and were conspicuous only in animals in which the pericardium had been securely sutured to the anterior chest wall at the time of the initial pericardiotomy. The dog's heart is more freely and more longitudinally suspended than is the human heart. The mediastinum, furthermore, is much less dense, less firm, and less rigid than is that of the human being. This may account for the lessened tendency to the production of adhesions which would cause systolic retraction. Systolic and diastolic shocks were often

palpable over the dog's precordium. Although these palpatory phenomena, especially the diastolic shocks, were common, they cannot be considered as pathognomonic signs. The pulse was frequently found to be of a distinct paradoxical type, but it was not invariably so and

Fig. 1.—Chronic adhesive pericarditis. Anterior and posterior views of the excised heart of dog No. 115, with the pericardium slit and stripped back to show the firmness and extent of the adhesions between the parietal and visceral pericardium.

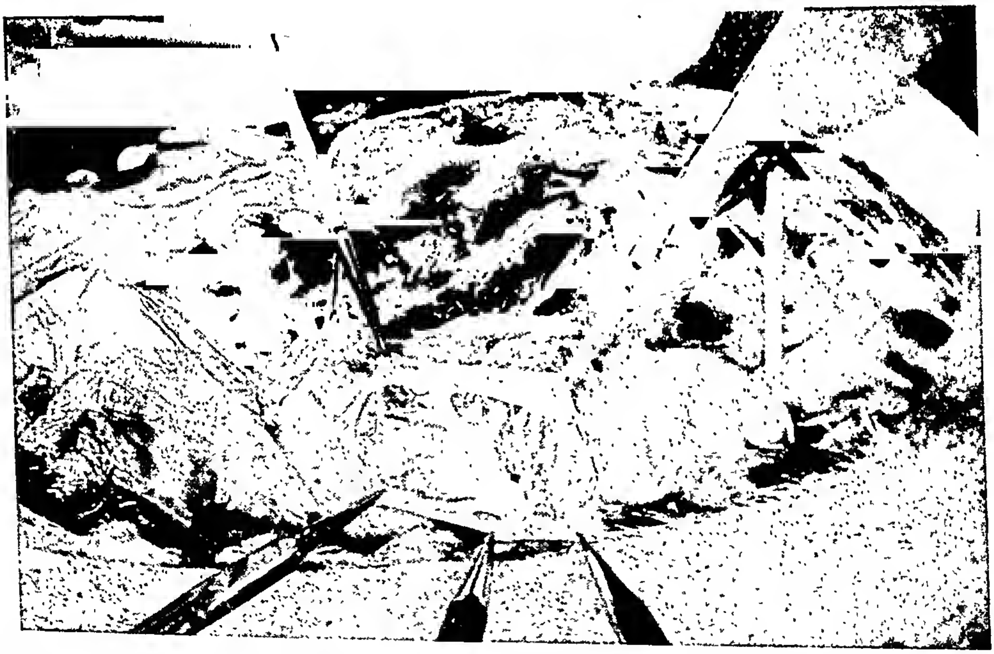

Fig. 2.—Chronic adhesive pericarditis. View of the heart of dog No. 185, in situ, with the pericardium split, dissected back, and pulled away by the five attached mosquito forceps.

the sign was absent in many dogs in which complete synechia of the pericardium was present (Figs. 1, 2, 3, 4).

Electrocardiographic findings (Fig. 5) were of definite significance only when fixation of the electrical axis in all three standard positions was positively established. The shifts, however, probably because of the position and suspension of the heart of the dog, are slight in some

normal dogs, and doubling the sensitivity of the string of the galvanometer is often necessary to demonstrate differences in the heights of the complexes. This in itself greatly distracts from the value of electrocardiographic studies under the experimental conditions. We

Fig. 3.—Chronic adhesive pericarditis and mediastinitis. Anterior mediastinum and heart in situ of dog No. 206, showing the extent of the mediastinal fibrosis and the parietal adhesions that the dogs in group IV had along with obliteration of the pericardial cavity.

were able to find definite fixation only when extrapericardial as well as intrapericardial adhesions were present. This is what one might expect. It was, however, common to find some anterior adhesions and complete synechia pericardii in dogs that had shown definite shifting

of the electrical axis. These discrepancies must be accounted for by the thinness of the dog's mediastinum and the peculiar suspension of the dog's heart with the long axis more nearly in a sagittal plane.

In our opinion, these discouraging results as to the value of the electrocardiographic sign of fixation of the electrical axis in adhesive pericarditis cânnot be considered to hold true in the case of human beings. The suggestion may, however, be accepted that there is necessity for caution in the interpretation of the finding of fixation of the electrical axis described by Dieuaide and Carter as pathognomonic in itself of adherent pericardium. The diagnosis should not rest on the electrocardiographic sign only, and, of course, this would rarely be the

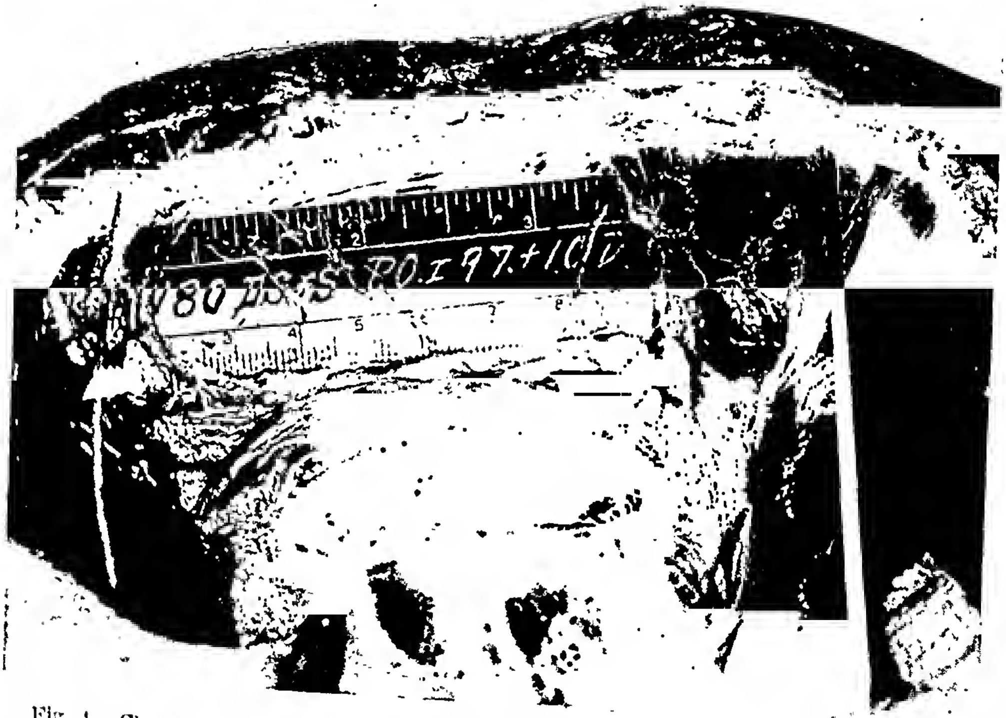

Fig. 4.—Chronic adhesive pericarditis without mediastitis. Transparent, filmy, diaphanous veil of the normal anterior mediastinum as it was perserved in the dogs of group V that otherwise had had complete pericardial obliteration experimentally produced.

case for usually there are other physical signs present which suggest the special electrocardiographic study in the three positions, for the routine procedure is to take the curves in one position only. It must be admitted, however, that the electrocardiographic findings in respect to the electrical axis are much more significant in humans. The human mediastinum, as is well known, is a denser, firmer, and more rigid tissue than the mediastinum of the dog, and the human heart is more transversely placed, rests on the diaphragm, and comes closer to the anterior chest wall.

The fluoroscopic studies yielded some interesting data, which the roentgenograms (Fig. 6) failed to show. We attempted to record

graphically, by means of moving pictures and by the roentgenographic slit method, the movement of the left heart border. Our attempts have been unsuccessful thus far. We have, however, noted a very definite change in the movements of the left cardiac border, especially in the region of the auriculoventricular groove where there is normally to be seen under the fluoroscope the see-saw movement with the fulcrum in the auriculoventricular groove at its extreme left end.

THE HEART WEIGHTS AND RATIOS IN THE EXPERIMENTAL ANIMALS WITH ADHESIVE PERICARDITIS

Observations on Hypertrophy.—The body weight of the animal was recorded. After noting the gross external adhesions at autopsy, the heart was removed and freed of blood. The vessels were cut flush

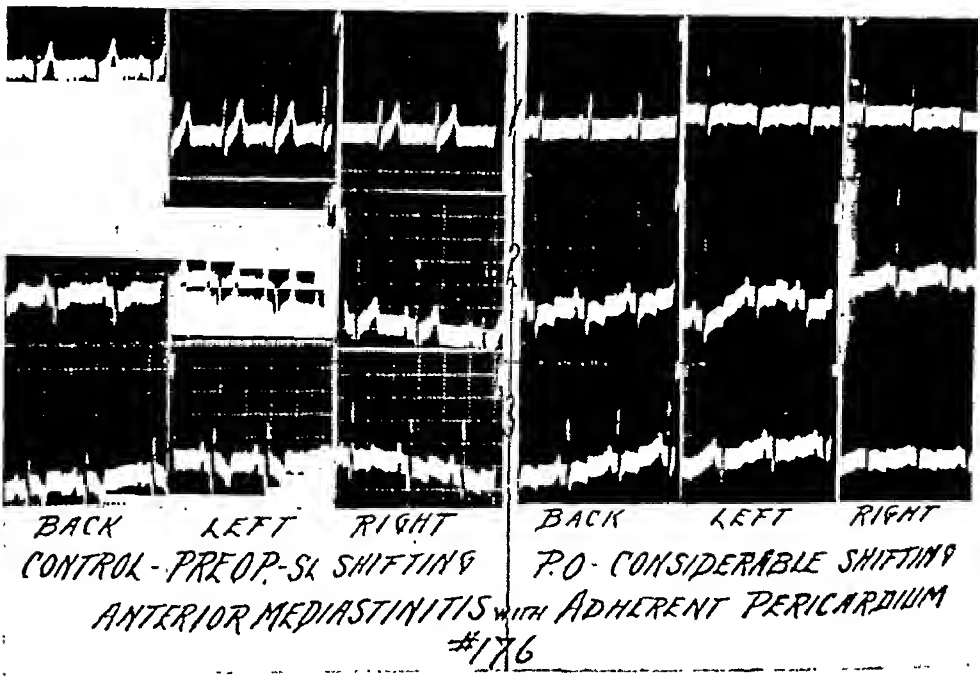

Fig. 5.—Electrocardiograms of dog No. 176 with the Leads I across the top, Leads II in the middle horizontal row, and Leads III in the bottom row. The first three columns to the left represent the three control leads, respectively, taken on the back, on the left side, and on the right side. Only slight shifting is present, as evidenced by the slight differences in heights of the R-waves in the three positions. The three columns to the right represent the curves taken after the production of a chronic mediastinopericarditis. It will be seen that the differences in heights of R-waves, especially in Lead I, are much greater, which indicates even increased shifting of the electrical and, supposedly also, the anatomical axis.

with the auricles and the semilunar cusps and the heart fixed according to the standard formalin procedure.[3] The kidneys and spleen were removed and their weights recorded.

The heart capacities and ventricular thicknesses were measured, and the heart was divided by the midseptal method and by Lewis' method. The ratios of the left ventricle weight to that of the right ventricle and

of the whole heart to the body weight were established. These figures are recorded in the accompanying tables, which will be here summarized.

Table I shows that there are practically no changes from the ratios for normal dogs in the values for the L/R ratio of the left ventricular weight to the right ventricular weight and of the total heart weight to the body weight (HW/BW) ratios of dogs with acute purulent pericarditis and mediastinitis lasting from eight to three days. This indicates that these acute lesions for short periods are not associated with a response by hypertrophy on the part of the heart. These dogs make an excellent control series.

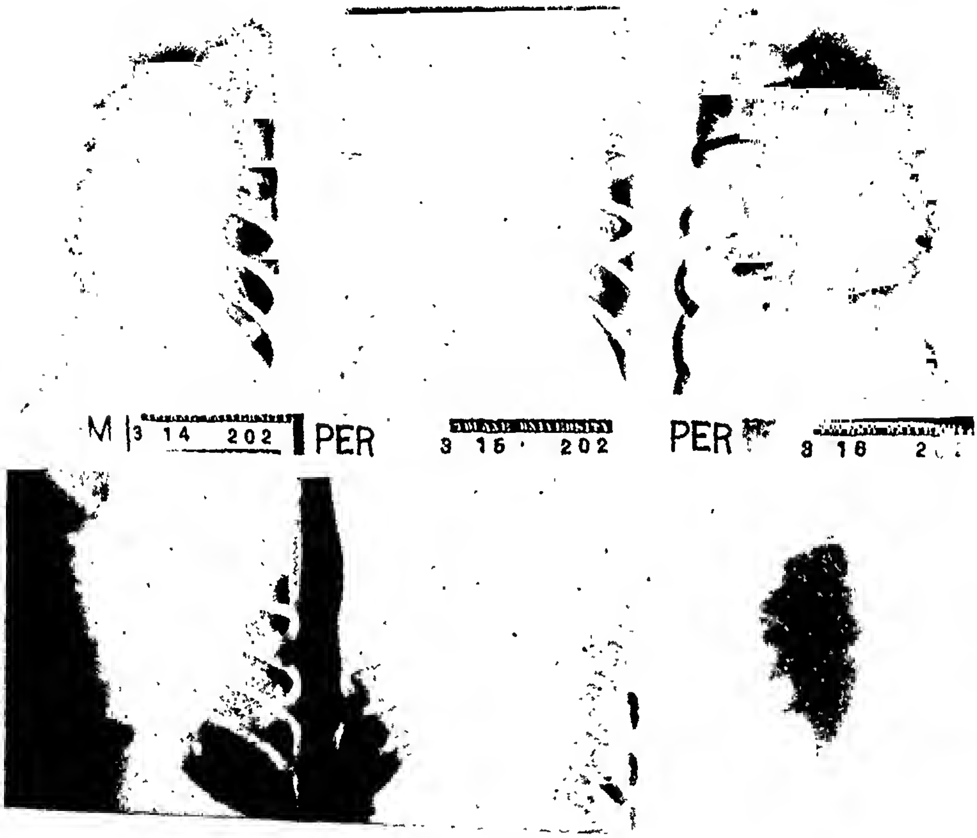

Fig. 6.—A short series of roentgenograms showing how the enlarged shadow of the acute pericardial effusion decreases and the gradual slight cardiac enlargement supersedes.

TABLE I

ACUTE PURULENT PERICARDITIS WITH ACUTE MEDIASTINITIS

DAYS	L/R	HW/BW	DAYS	L/R	HW/BW
8	1.635	0.0099	3	1.105	0.0086
8	1.500	0.0081	3	1.088	0.0093
6	1.582	0.0088	3	1.037	0.0097
6	1.300	0.0085	3	1.092	0.0099
4	1.057	0.0089			
Average				1.081	0.0090
Normal				1.398	0.0080

Table II contains the heart data from 5 dogs in which there were external adhesions but no internal fibrous pericardial bands. These show no conspicuous changes from the normal except for a slight tendency to right ventricular preponderance. Apparently this type of lesion embarrasses the heart the least of any of the chronic lesions studied. The last two dogs were studied in conjunction with Dr. Alton Ochsner. These two dogs had had complete synechia, which was relieved by a secondary operation and the re-formation of the fibrous adhesions prevented. This was accomplished by the application of a digestant solution after cardiac decortication by digital separation of the adherent pericardial layers. The changes were not conspicuous.

TABLE II

CHRONIC ANTERIOR MEDIASTINITIS WITH THE EPICARDIUM UNINVOLVED

NO.		TOTAL DAYS	L/R	HW/BW
127		516	1.100	0.0085
128		200	1.075	0.0092
120		31	1.500	0.0092
122		11	1.329	0.0091
	PO_1 + PO_2			
169	107 + 14	121	1.210	0.0093
177	91 + 5	96	1.082	0.0097
Average			1.216	0.0092
Normal			1.398	0.0080

PO_1—Length of time after the first operation.
PO_2—Length of time after the second operation.

Table III shows the effect on the heart weights and ratios of anterior mediastinal adhesions associated with partial synechia of the pericardium. Under these conditions the dogs that had the lesions for more than eighty days showed distinct cardiac hypertrophy with a definite increase in the preponderance of the right ventricular weight. As a matter of fact, in the animals that lived long there was actually a larger right than left ventricle.

TABLE III

PARTIAL PERICARDIAL OBLITERATION WITH MEDIASTINITIS

NO.	DAYS	L/R	HW/BW
124	502	0.885	0.0133
130	212	0.978	0.0100
147	108	1.000	0.0130
149	83	1.062	0.0131
132	81	1.360	0.0079
195	55	1.135	0.0078
125	43	1.223	0.0096
202	34	1.161	0.0084
Average		1.101	0.0101
Normal		1.398	0.0080

Table IV presents the heart weight ratios from dogs that had had complete synechia of the pericardium along with anterior medias-

tinitis. These dogs showed the greatest degree of general hypertrophy and also right ventricular preponderance. In all instances where the lesion had been present more than thirty-five days, definite evidence of hypertrophy was revealed.

TABLE IV

COMPLETE PERICARDIAL OBLITERATION WITH MEDIASTINITIS

DAYS	L/R	HW/BW	DAYS	L/R	HW/BW
331	0.641	0.0155	42	1.144	0.1008
252	0.773	0.0204	37	1.180	0.0120
221	1.150	0.0133	35	1.000	0.0140
116	1.180	0.0117	33	1.078	0.0092
111	1.056	0.0114	33	0.963	0.0083
97	1.107	0.0091	17	1.070	0.0116
62	1.200	0.0103	16	1.250	0.0094
45	1.200	0.0100	13	1.058	0.0086
Average				1.162	0.0116
Normal				1.398	0.0080

Table V is made up of data from dogs that had had complete synechia of the pericardium (for varying periods of days) which embarrassment was relieved by a secondary operation done in association with Dr. Alton Ochsner, and the dogs sacrificed at intervals after the second operation. These animals showed less evidence of the cardiac response of hypertrophy. The results, however, though less conspicuous, still correspond in general to our findings in Table VI. The animals had for the most part relatively slight mediastinitis and in this way resembled those in Table VI.

TABLE V

COMPLETE PERICARDIAL OBLITERATION WITHOUT AND WITH SLIGHT MEDIASTINITIS. ALL SECONDARILY OPERATED UPON

NO.	PO_1		PO_2	TOTAL DAYS	L/R	HW/BW
169+	107	+	14	121	1.210	0.0093
177+	91	+	5	96	1.082	0.0097
176	97	+	10	107	1.200	0.0076
195	45	+	10	55	1.134	0.0078
197	30	+	18	48	1.150	0.0072
203	14	+	21	35	1.040	0.0070
192	25	+	7	32	1.099	0.0096
Average					1.125	0.0085
Normal					1.398	0.0080

PO_1—Length of time after the first operation.
PO_2—Length of time after the second operation.

Table VI contains the heart data of dogs that had had internal pericardial adhesions only for varying periods of days. It is of considerable significance inasmuch as the dogs in the series were operated upon in association with Dr. Alton Ochsner, whom we called upon for help in obtaining complete obliteration of the pericardial cavity without any mediastinitis whatsoever. The L/R and HW/BW ratios are

Table VI

Complete Pericardial Obliteration Without Mediastinitis

DAYS	L/R	HW/BW	DAYS	L/R	HW/BW
107	1.113	0.0086	34	1.048	0.0084
90	1.095	0.0123	28	1.030	0.0093
60	1.358	0.0120	25	0.912	0.0095
50	1.000	0.0120	25	1.142	0.0070
37	1.200	0.0105	14	0.955	0.0084
34	1.160	0.0084			
Average				1.092	0.0097
Normal				1.398	0.0080

similar to those of Table V and are interesting in that they show a distinctly less degree of cardiac hypertrophy and of right ventricular hypertrophy than we encountered when, in addition to the intrapericardial adhesions, there was also extrapericardial anchorage (Table IV). We did not find, however, as might be expected from clinical reports, cardiac atrophy.

The averages for the heart weight ratios of the various groups are brought together to facilitate comparison of the effects of the various experimental procedures.

Composite Table

Experimental Pericarditis

	Average L/R	Average HW/BW
I. Ac. Pur. Per. with Med.	1.081	0.0178
II. Chr. Ant. Med. without Per.	1.216	0.0091
III. Part. Per. Obl. with Med.	1.101	0.0104
IV. Comp. Per. Obl. with Med.	1.162	0.0116
V. Comp. Per. Obl. without Med.	1.092	0.0097
VI. Comp. Per. Obl. without and with Sl. Med.—Reoperated	1.125	0.0085
Normal	1.398	0.0080

SUMMARY AND CONCLUSION

We have been able experimentally to reproduce at will in dogs the various types of chronic fibrous pericarditis which are encountered clinically.

The animals with chronic adherent pericarditis presented no pathognomonic clinical signs, except perhaps the localized systolic tugging in instances in which the parietal pericardium had been anchored to the intercostal muscles.

Electrocardiographic evidence of fixation of the electrical axis was, much to our disappointment, not uniformly present. This, however, may be due in part to peculiarities of the mediastinum and the midline suspension position of the heart in the dog.

After the production of an obliterative pericarditis fluoroscopic studies revealed a rather striking change in the character and movements

of the left heart border, especially in the region of the auriculoventricular junction. A graphic record of this changed movement may be of some diagnostic significance.

The gross pathological studies in regard to cardiac hypertrophy more or less confirmed our previous conceptions. The greatest degree of cardiac hypertrophy was found in the group in which chronic mediastinal and parietal adhesions as well as adhesive pericarditis were present. The tugging of the heart bound by fibrous bands from the firm structures of the chest is apparently most conducive to hypertrophy. The dogs with partial obliteration of the pericardial and mediastinal and parietal adhesions showed the second greatest degree of hypertrophy. Complete synechia of the pericardium with slight or with no mediastinal fibrosis showed hypertrophy but of less degree than the other types of chronic mediastinopericarditis.

The feasibility of digital separation of pericardial adhesions and the prevention of the re-formation of adhesions have been proved, and clinical and pathological evidences of benefit in the experimental animal have been noted.

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HEART-BLOCK SHOWING MULTIPLE TRANSITIONS ASSOCIATED WITH CONVULSIVE SYNCOPE: REPORT OF A CASE WITH DETAILED HISTOPATHOLOGICAL STUDY

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FROM time to time, in medical literature, cases of complete heart-block have been recorded in which have been demonstrated gross or histopathological lesions that interfere with or completely obstruct the passage of the impulse through the auriculo-ventricular bundle (His). The incidence of such cases is so low that the publication of additional cases is justified.

Lesions of various kinds have been described and notable among them have been gummas.[2, 3, 4, 6, 9, 12, 13, 14, 21, 28, 34, 35, 40] Areas of calcification that encroach on or destroy the continuity of the bundle have been recorded by some observers.[7, 8, 15, 17, 25, 29, 31, 38, 39] In other cases, obliterative disease of the branches of the coronary arteries which supply the region of the bundle has been described.[10, 29] Fibrosis of the auriculo-ventricular bundle likewise has been observed.[11, 16, 23, 36, 39] Fatty infiltration of the bundle, and also simple lymphocytic infiltration,[17] occasionally have been noted.[5, 30] In a few cases, infarction of the heart near, or in, the interventricular septum has resulted in complete heart-block.[20, 27, 41] Involvement of the auriculo-ventricular bundle by ulceration associated with mural endocarditis has been noted.[19] A few instances of tumors of the septum causing obstruction or destruction of the bundle have been reported. These tumors comprise endothelioma,[1] round-cell sarcoma,[26] and fibroma.[37] In a few cases in which complete heart-block existed, a lesion of the bundle was not demonstrated.[18, 22, 32, 33]

The case which constitutes the basis of this report presented some extremely interesting and unusual features.

CASE REPORT

A man aged seventy-four years presented himself for examination because of fainting spells. His health up to three and a half years before had been good. Previous illness of all types was denied. He had two grown children, living and

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well. Three and a half years before, during a general examination which was conducted owing to the presence of an inguinal hernia, the systolic blood pressure was found to be 190 and the diastolic 110. Cardiovascular symptoms were not elicited, and the patient was active for his age. Three months before the last examination he began to have dizzy spells, occasionally associated with momentary unconsciousness. These attacks gradually increased in frequency until the time of his visit to The Mayo Clinic; their average occurrence was two or three times a day.

The heart was enlarged; the total area of dullness was about 16 cm. The rate was slow, only 40 each minute. The aortic second sound was accentuated. The peripheral arteries were distinctly palpable and sclerotic. The systolic blood pressure was 240; the diastolic, 105. The lungs were slightly emphysematous and a few moist râles were audible at the bases. Repeated urinalyses were negative. The hemoglobin was 69 per cent (Dare), the erythrocytes numbered 4,560,000, and the leucocytes, 8,800 for each cubic millimeter. Roentgen-ray studies of the chest verified the fact of cardiac enlargement.*

The diagnosis made was high grade heart-block with convulsive syncope, essential hypertension, and generalized arteriosclerosis. The patient died during a seizure of convulsive syncope.

PATHOLOGICAL EXAMINATION

Necropsy.—The viscera of the chest and abdomen were examined. Since the heart was the organ of interest, the other data will be merely summarized. The other organs appeared grossly and microscopically normal except for the presence of a chronic cholecystitis and cholelithiasis, marked arteriosclerosis of the aorta and large arteries, bilateral hydrocele, and the site of an ancient right inguinal herniotomy with local healed fibrous peritonitis.

The heart weighed 388 gm. On the posterior wall of the right ventricle were two small "soldier's patches," and, on the anterior surface, was a larger, irregular patch measuring roughly 5.0 by 1.5 cm. The epicardial fat was normal in amount. The muscle was grayish-brown, firm, and on tangential section did not show abnormal streaking. The chambers were not dilated and the walls were not hypertrophied. The valves were functionally normal, and the endocardium in general appeared normal. The foramen ovale was closed. Beneath the attachment of the posterior cusp of the mitral valve was felt a number of calcareous deposits, not continuous with one another and not of large size. Bulging out beneath the point of insertion of the anterior leaflet of the mitral valve in the membranous septum was an elongated, irregular cauliflower-like calcareous mass just at the juncture of the membranous and muscular portions of the interventricular septum and embedded in the muscle of the septum. The part which was visible and projecting was about 0.9 cm. in diameter. When the interventricular septum was palpated along the juncture of the membranous and muscular portions, this visible calcareous mass was felt to be continuous with a rigid deposit of calcium of smaller diameter than the projecting mass. This rigid deposit ran toward the right just below the juncture of the membranous with the muscular portion of the septum, becoming gradually smaller, and ending just beneath the middle of the attachment of the right coronary cusp of the aortic valve. On the right side the calcareous mass was felt to project out into the right ventricle prominently beneath the point of juncture of the septal and anterior leaflets of the tricuspid valve, but it was covered by the endocardium and not visible. Fig. 1 is a full-size roentgenogram of the opened heart showing the left side of the interventricular septum with

*The electrocardiographic studies are recorded elsewhere.

the calcium deposit just described. The line of attachment of the aortic cusps is outlined with ink. The visible mass of calcium at the insertion of the anterior cusp of the mitral valve is outlined in ink, while the calcium embedded in the upper end of the muscular portion of the septum is not outlined and is seen extending across to the middle of the attachment of the right coronary cusp of the aortic valve. On the right side of the picture is seen an irregular opacity which is due to the calcium lying beneath the insertion of the posterior leaflet of the mitral valve.

The mitral valve appeared normal except for its association with these calcium deposits. The corpus arantii of the noncoronary cusp of the aortic valve was elongated laterally and thickened, and gave rise to a number of small fibrous processes. The tricuspid and pulmonary valves appeared normal. There was mild atheromatosis of the root of the aorta with one small subintimal calcified plaque,

Fig. 1.—Roentgenogram (full size) of the opened heart through the interventricular septum from the left side, showing the mass of calcium. The portion of the mass which is visible to the unaided eye is outlined with ink. The aortic cusps are also outlined with ink.

0.4 cm. in diameter. The orifices of the right and left coronary arteries appeared normal, but beside each was a small orifice of an independent branch of each artery. There was moderate atheromatosis of both main coronary arteries without notable reduction of the size of their lumina; the smaller branches, however, seemed to be constricted.

Microscopical Examination of the Heart.—Twelve blocks of tissue were removed from the heart for microscopical examination, as follows: (1) one block including the sino-auricular node, which lies beneath the epicardium, in the sulcus terminalis, just below the superior vena cava; (2) three blocks through the auriculo-ventricular and interventricular septums to be described later, which include the main portions of the conduction system; (3) two blocks transversely across the interventricular septum on the left side near the base, which include the main ramifications of the

left bundle-branch; (4) one block from the trabeculum which corresponds to the moderator band of the calf's heart and which normally contains the single right bundle-branch, and (5) one block each from the base of the right anterior papillary muscle, the interauricular septum just below the fossa ovalis, the left ventricle at the base posteriorly, and the posterior wall of the right ventricle midway between base and apex. A block was removed also from the left ventricle, to be stained for fat.

Transverse sections, 10 microns thick, were made at frequent levels through the block which contained the sino-auricular node and were stained with hematoxylin and eosin and with van Gieson's stain. The endocardium and epicardium were not thickened and did not show evidence of inflammation. The sino-auricular node with its special artery appeared normal in respect to the amount of fibrous tissue and the details of the specialized interlacing muscle cells. The arterioles of the node

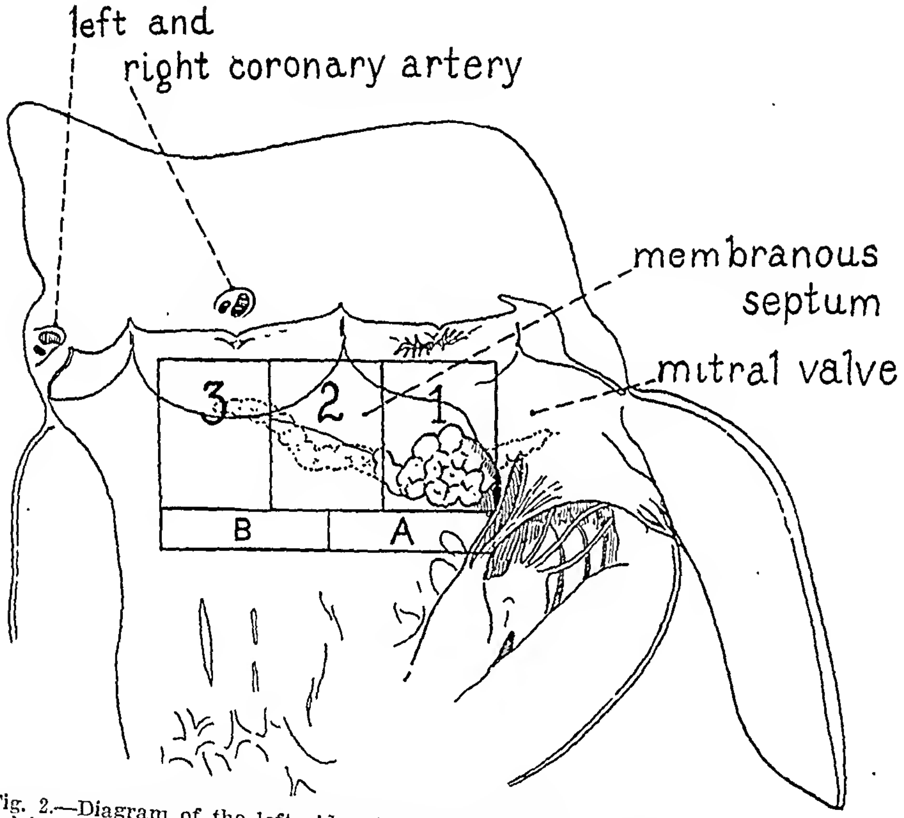


Fig. 2.—Diagram of the left side of the interventricular section, showing the mass of calcium (invisible portion in dotted line) and the site of the blocks of tissue *1*, *2*, and *3* and *A* and *B*.

were not thickened. There were a number of nerves in the vicinity of the node, two of which seemed to be entering the node. The ordinary heart muscle fibers appeared normal, although somewhat distorted as usual, due to the shrinkage during fixation of the large amount of subepicardial fat in this region. The myofibrillae stood out prominently and the cross striations were indistinct and interrupted, but this is the usual appearance of the muscle fibers in the right auricle where fat is excessive. The walls of the blood vessels were not thickened.

The auriculo-ventricular node and bundle were included in Blocks 1 and 2, as indicated in the diagram (Fig. 2) which shows the upper part of the left side of the interventricular septum and root of the aorta. Block 3 contained the main part of the left bundle-branch. Serial sections were made transversely through these three blocks from right to left as one looks at the diagram. Block 1 con-

tained part of the auricular and of the auriculo-ventricular septums and in it were the auriculo-ventricular node (node of Tawara) and the beginning of the bundle of His. Block 2 included part of the membranous and part of the muscular portions of the interventricular septum in the middle area; this contained the main part of the auriculo-ventricular bundle and the origin of both main branches. Block 3 included part of the muscular portion of the septum and the middle third of the right coronary cusp of the aortic valve; it contained part of the left main branch of the bundle. The blocks were decalcified and embedded in paraffin. The sections were cut 10 microns thick, and every twenty-sixth, twenty-seventh, and twenty-eighth section was mounted and stained with hematoxylin and eosin; the twenty-ninth, thirtieth, and thirty-first sections were mounted and stained with van Gieson's preparation. The intervening sections were retained but not mounted or stained except as desired.

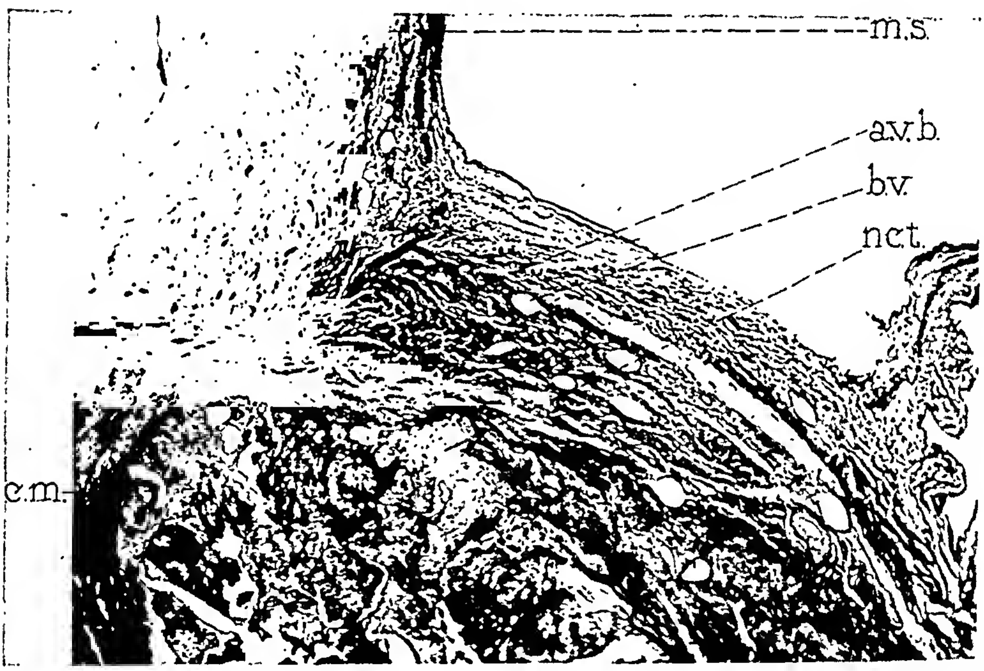


Fig. 3.—Oblique section of the auriculo-ventricular (His) bundle between the auriculo-ventricular node and the bundle-branches, showing the mass of calcium pressing against it from below (x22); *m.s.*, membranous septum; *a.v.b.*, auriculo-ventricular bundle; *b.v.*, blood vessels in the bundle; *n.c.t.*, new connective tissue between the bundle and the mass of calcium; *c.m.*, calcium mass.

In all of the sections of Blocks 1 and 2 the calcium was present, gradually thinning out in Block 3. The heaviest deposit was in Block 1. It was about 0.6 cm. in diameter at each end, but in the middle it was more extensive because of the portion which protruded into the left ventricle. In the sections, the calcium in Block 1 was seen to be deposited mainly in the ventricular muscle, between the right auricle, above, and the ventricular septum, below, causing the wall of the septum to bulge out on both sides. It was prominent at the base of the aortic attachment of the mitral valve in the substance of which also was seen a little deposit of calcium in one area. The accumulation of calcium was irregular in outline on cross-section and was lobulated; in the main it was enclosed in a capsule of variable thickness composed of dense, collagenous, fibrous tissue. Trabeculums of this capsule were seen in places between lobules of the calcium. The muscular tissue had been pushed aside and at the edges of the deposit of calcium it appeared to be compressed. In some places, narrow strands of muscle fibers formed

a band around the edge of the calcium and were surrounded by or embedded in the fibrous capsule. Between the lobules of the calcium, here and there near the edge of the mass, was a patch of delicate fibrous connective tissue in which were a few small lymphocytes and some plasma cells; these cells were more numerous in some areas than in others. In Block 3 the deposit extended across the interventricular septum at the juncture of the membranous and muscular portions and caused a large hump on the right side in the region of the juncture of the septal and anterior leaflets of the tricuspid valve. The deposit continued in Block 3 until it reached the attachment of the right coronary cusp of the aortic valve, where it thinned out and was lost just above the point of insertion of the cusp in the aortic ring. At the juncture of Blocks 2 and 3 the calcium deposit was about 0.4 cm. in diameter.

In Block 1 just at the base of the mitral valve was a large area of delicate connective tissue with many thin-walled vessels and some small lymphocytes and plasma cells. Where the calcium deposit was heaviest at the base of the valve,

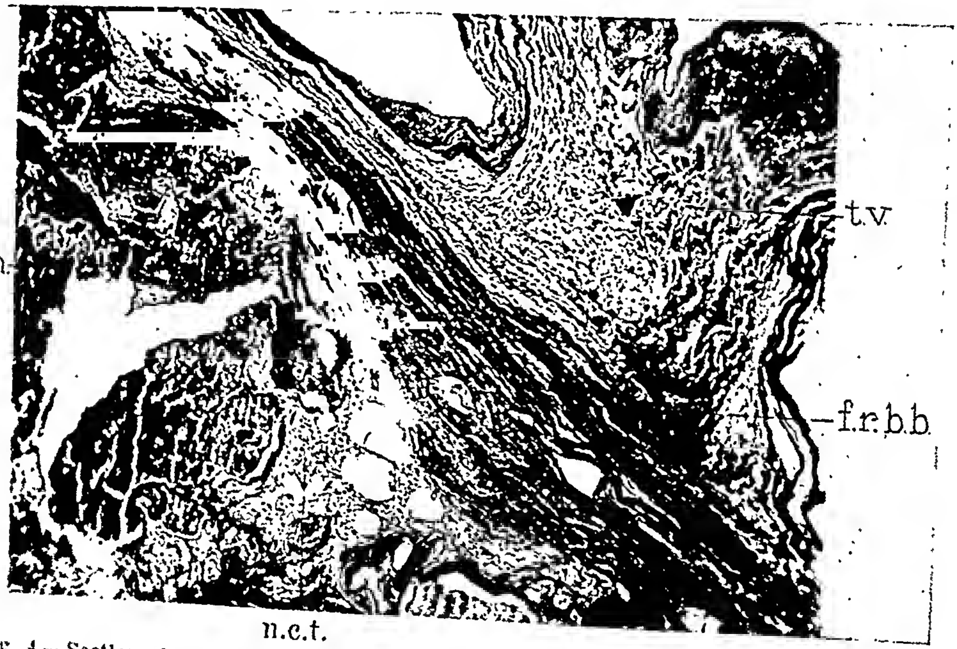


FIG. 4.—Section showing the first part of the right bundle-branch cut almost longitudinally (x36); *t.v.*, tricuspid valve; *f.r.b.b.*, fibrosed right bundle-branch; *n.c.t.*, new connective tissue with plasma cells and small lymphocytes between the bundle-branch and the mass of calcium; *c.m.*, calcium mass.

this connective tissue became more compact and contained smooth muscle fibers from the endocardium and more numerous small lymphocytes and plasma cells. In the middle of this block the central fibrous body began to appear, below and on the left side of which the calcium abutted with a little of the ventricular musculature interposed. No part of the conduction system was recognized until the five hundred twenty-eighth section of Block 1 was reached, where the right edge of the auriculoventricular node was seen; nevertheless, the branch of the right coronary artery which was crossing the lower part of the right auricle to supply the node had been seen in the previous sections. The only abnormal artery was noted in the region of the right end of the node. This was a small artery with a very thick muscular wall and a small lumen, situated at the right side of the central fibrous body and later turning downward and running between the central fibrous body and the node. The node was seen in the sections from the five hundred twenty-eighth to the eight hundred seventy-fourth. It was apparently normal and was formed as

usual by compact whorl-like masses of small Purkinje fibers with a delicate interstitial fibrous connective tissue. One large artery and a number of smaller ones were in the node. In the region of the eight hundred seventy-fourth section the node passed into the bundle of His and the fibers became more nearly parallel. The calcium now came to lie more below than on the left side of the bundle, but the latter was for a distance still on the right side of the central fibrous body. In the first sections of Block 2, the bundle was longer transversely than from above downward (Fig. 3). It contained several small blood vessels cut transversely. Below the bundle, and nearer the left side, the calcium was separated from the bundle by very little fibrous tissue and a bit of the calcium projected slightly upward into the bundle. Just to the right of the projection was an area of delicate connective tissue containing a number of thin-walled blood vessels and some plasma cells and small lymphocytes. The deposit of calcium was now pushing out the membranous septum toward the left. A little farther along the area of delicate connective tissue became larger and was interposed between the calcium and the

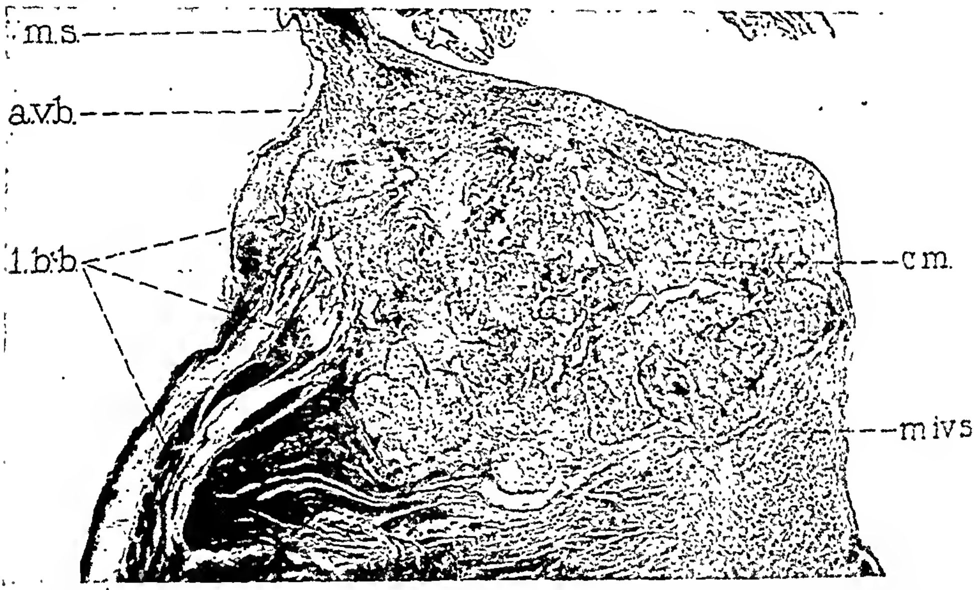


Fig. 5.—Cross-section through upper portion of interventricular section showing the end of the crus communis and the left bundle-branch in relation to the mass of calcium (x12). *m.s.*, membranous septum; *a.v.b.*, bundle of His, considerably fibrotic; *l.b.b.*, left bundle-branch, the upper portion of which is invaded and almost replaced by fibrous connective tissue; *c.m.*, calcium mass; *m.iv.s.*, muscular portion of interventricular septum.

bundle. The small lymphocytes were at first more numerous. Soon, however, the plasma cells became more abundant and the small lymphocytes scarce. The Purkinje fibers of the bundle were considerably shrunken and distorted due to decalcification and fixing, but otherwise appeared normal. Between the sixty-third and four hundred third sections of Block 2, the bundle expanded toward the right and gave origin to the right main branch (Fig. 4). The branch itself, however, was traceable only as far as the right side of the lump formed in the wall of the right ventricle by the mass of calcium where its pathway seemed to be obstructed by dense fibrous tissue. Between the two sections mentioned, the main bundle became progressively flatter, as though compressed from below by the calcium mass. Also it became more fibrous and was replaced, at its left side, first by fibrous tissue and then by a nodule of calcium. In sections near the three hundred sixty-first the bundle was very flat, very fibrous and almost obliterated. From the four hundred fourth section on, the bundle passed through the membranous septum to the left side, forming

at first the triangular crus communis as it lay in the base of the membranous septum. The crus communis was separated from the subjacent ventricular muscle by the calcium; it was very fibrous and contained a large number of round spaces, evidently blood channels. The fibrosis was most marked at its base adjacent to the calcium mass. The bundle became gradually larger, but this increase in size was due to a greater fibrous content, whereas the muscle elements became scantier. The origin of the left main branch was soon seen and could be traced through several hundred sections. The bundle and the beginning of the left main branch came to be invaded by a few small lymphocytes. By the time the six hundred fifty-second section was reached, the bundle had become replaced almost entirely by fibrous tissue and the origin of the left branch passed through a large area of fairly delicate connective tissue which contained many relatively large blood spaces and some small lymphocytes (Figs. 5 and 6). From this point on, the left branch was seen lower down, to the left of and below the mass of calcium until it was

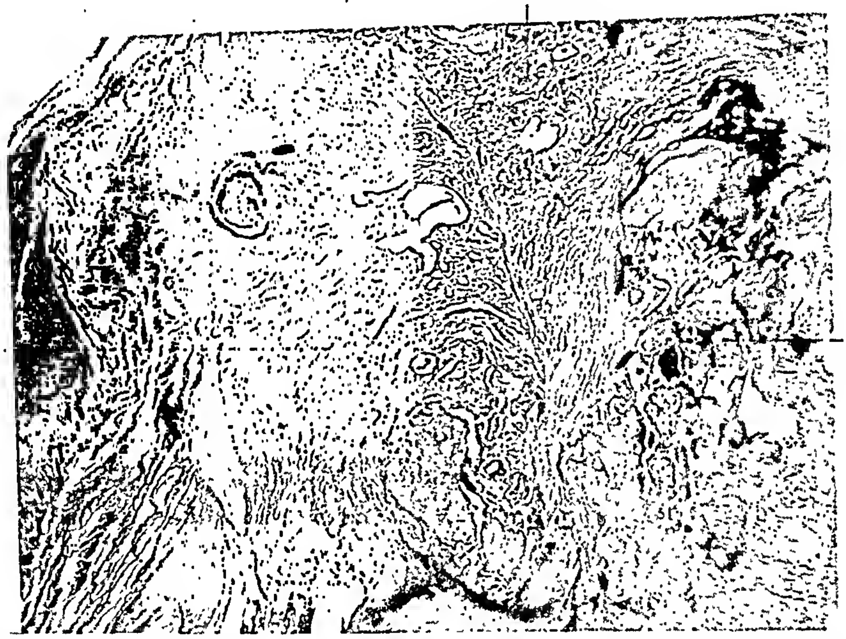


Fig. 6.—Greater magnification (x33) of portion of preceding section showing the fibrotic bundle of His, *f.a.v.b.*; the large area of delicate connective tissue through which the left bundle-branch, *f.l.b.b.*, passes; and the calcium mass, *c.m.*

no longer present in the sections beyond the four hundred ninety-sixth of Block 3. The left branch itself appeared normal. The deposit of calcium in Block 3 was surrounded by a thicker capsule of dense fibrous tissue, which extended downward for a distance into the ventricular muscle.

Of the two blocks of tissue removed from the left side of the interventricular septum near the base and cut transversely, that nearer the right (Block B, Fig. 2) showed the fibers of the left bundle-branch at the point where they were spreading out. In these sections the Purkinje fibers were seen both in transverse and longitudinal section, directly beneath the endocardium, and appeared normal.

The transverse sections of the moderator band failed to reveal any recognizable elements of the Purkinje system. that is, the right bundle-branch. But in the transverse sections of the base of the right anterior papillary muscle, two bundles of fibers resembling Purkinje fibers were seen, one on either side, embedded in a large amount of fatty connective tissue. The fibers themselves appeared normal but the large amount of fatty connective tissue was distinctly abnormal.

The sections of the interauricular septum and the right and left ventricles showed the cardiac muscle fibers to contain considerable lipochromatic pigment at the nuclear poles, more marked in the ventricles than in the auricles. There was no increase in the interstitial connective tissue and there were no areas of fibrosis. The walls of the arterioles were not appreciably thickened nor were the lumina narrowed. The section stained with Sudan III showed a slight deposition of small fat droplets in the muscle fibers.

Summary of Pathological Examination.—There was a bar of calcium extending across the interventricular septum, at the juncture of the membranous and muscular portions, and embedded in the upper edge of the ventricular musculature. A large portion of the bundle of His was invaded by fibrous tissue, some plasma cells and small lymphocytes, and was almost obliterated in part. The origin of the right bundle-branch was quite fibrotic. The origin of the left bundle-branch passed through a large area of relatively young fibrous connective tissue. The conduction system apparently was not entirely interrupted at any point but its function was certainly markedly impaired by the invasion of fibrous tissue and probably also by compression from the mass of calcium. The cardiac muscle fibers contained polar lipochromatic material but there was no fibrosis, very little fatty degeneration was present and the arterioles were not appreciably thickened.

Comment.—The frequency and the severity of the seizures of convulsive syncope were prominent features of this case. In several of the attacks, death appeared to have occurred but temporary recovery ensued. From the time that death appeared imminent until death actually occurred, a period of fifty hours elapsed.

During one of the most marked seizures, complete cardiac asystole occurred for approximately four minutes. This seems almost unbelievable but is proved by the continuous electrocardiographic records obtained. A somewhat comparable example of prolonged asystole is found in the case reported by Levine and Matton in which ventricular fibrillation and asystole occurred for five minutes.

Ventricular asystole occurred at times associated with high grade block, on one occasion to a degree of 64:1 and again in association with complete cardiac asystole.

The correlation in this case of the clinical features and the pathological observations is of considerable interest.

DISCUSSION OF ELECTROCARDIOGRAMS

The electrocardiograms in this case revealed multiple transitions which ranged from periods of normal sinus rhythm through varying grades of block, to remarkably long periods of complete cardiac asystole.

At the time of the admission of the patient to the hospital, 3:1 partial heart-block was present (Fig. 7). The ventricular components in Leads I and II are normal in appearance, but in Lead III the QRS complexes are of very low amplitude and are notched.

On the following day (Fig. 8) 2:1 partial block was detected. The similarity of the general features between this electrocardiogram and the one obtained on the preceding day is apparent.

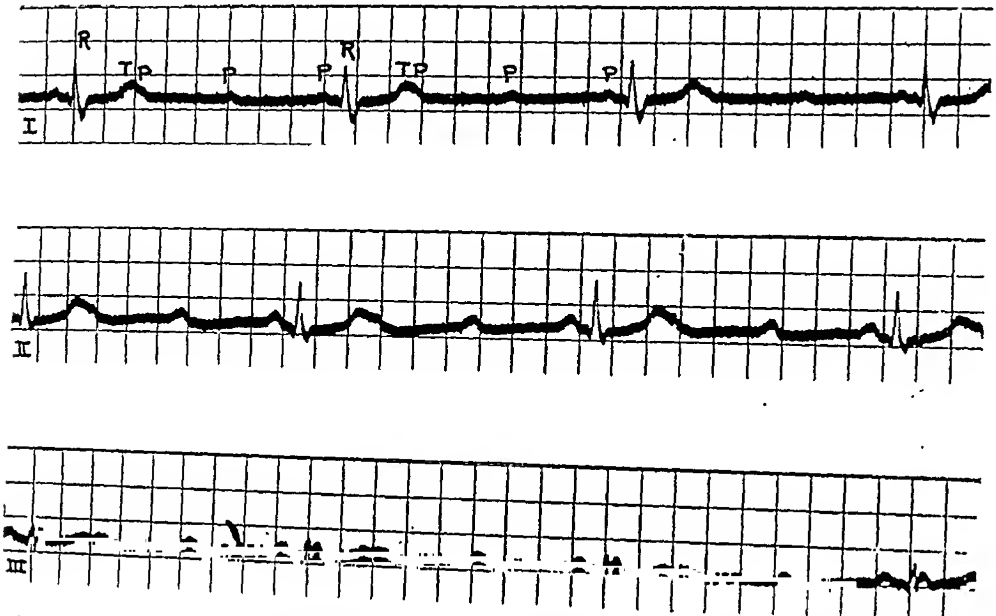


Fig. 7.—This record, taken in all leads, was obtained on the day of the patient's admission to the hospital. It shows the presence of 3:1 partial block.*

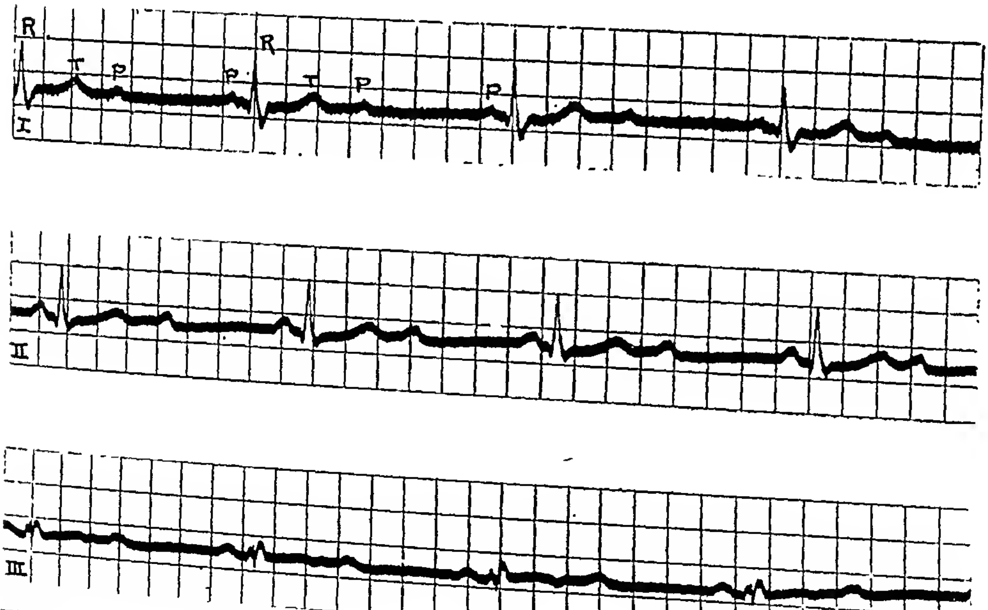


Fig. 8.—This record, taken in all leads, was obtained the following day (Fig. 7) and shows 2:1 partial block.

The records obtained two days later (Figs. 9 and 10) show the reëstablishment of normal sinus rhythm, occasionally interrupted by periods of block. These events are of interest in view of the pathological

*In all the records, the horizontal lines represent 1 millivolt and the vertical lines 0.2 second.

data; even though the auriculo-ventricular bundle was extensively involved, it was still able to conduct impulses in a normal manner for short intervals.

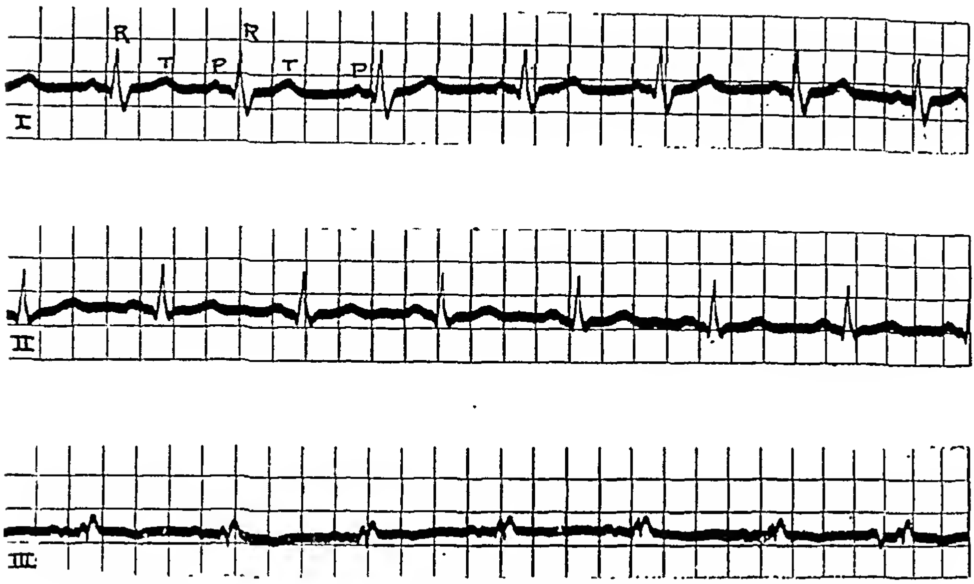


Fig. 9.—This record, also taken in all leads, was obtained two days later (Fig. 8) and shows the temporary restoration of normal sinus rhythm.

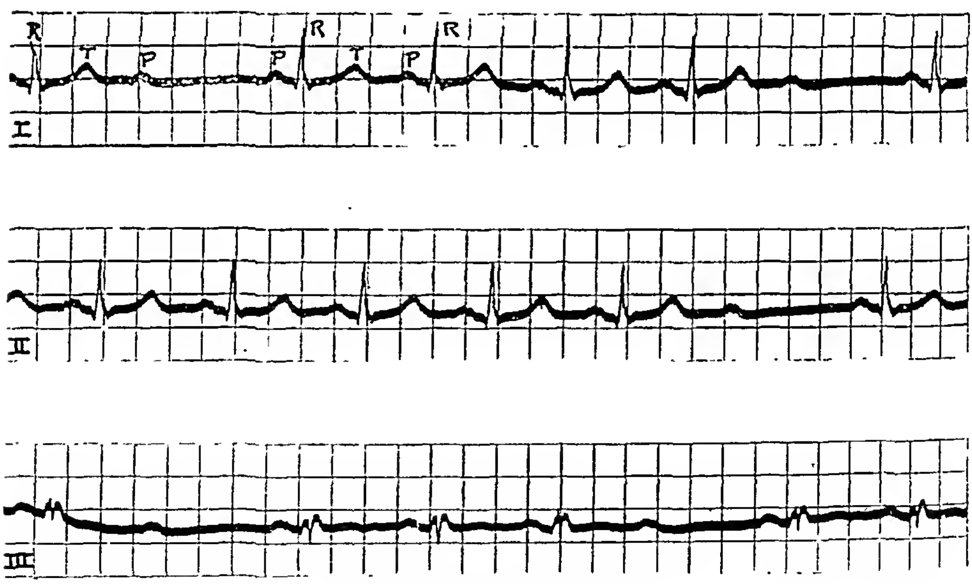


Fig. 10.—This record was obtained the same day (Fig. 9) and portrays sinus rhythm with periods of block.

The succeeding records (Figs. 11 to 26) were obtained about a week later, during the time when the seizures of convulsive syncope were extremely numerous. They were all taken in Lead II and are continuous strips.

All degrees of block are shown. In Figs. 11 and 12 are seen records of complete heart-block with varying ventricular complexes, indicative probably of changes in the point of origin of the idioventricular rhythm.

In Fig. 12 is shown the onset of a long period of ventricular asystole with high grade block, 22:1. In one electrocardiogram, a period of 64:1 block occurred. The diminution in the amplitude of the P-waves and the associated arrythmia are shown in Fig. 14.

Fig. 11.

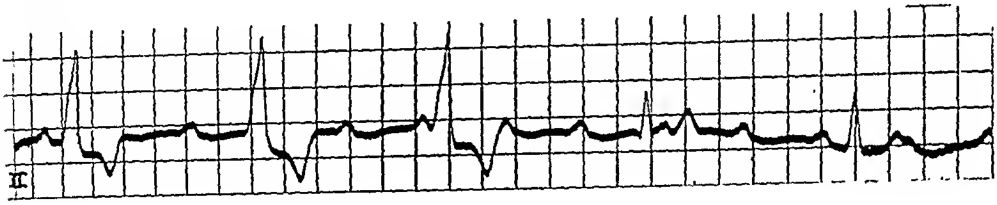


Fig. 12.

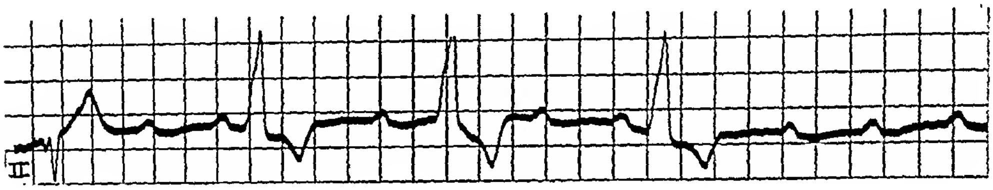


Fig. 13.

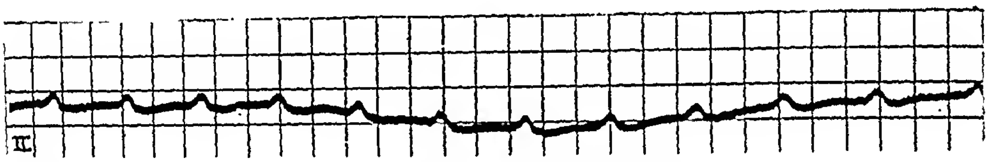


Fig. 11.—This record, and the following sixteen records, obtained about a week later than this one, are continuous strips taken in Lead II. They show many transitions, with some rather unusual features. In this record is shown complete heart-block with temporary aberration of the initial ventricular complexes.

Fig. 12.—This record is similar to the preceding one and shows the onset of a prolonged period of ventricular asystole.

Fig. 13.—This record exhibits a series of auricular waves only.

Fig. 14.

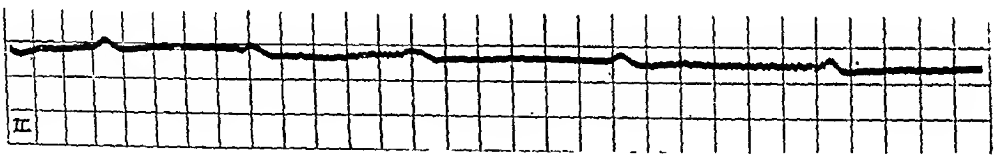


Fig. 15.

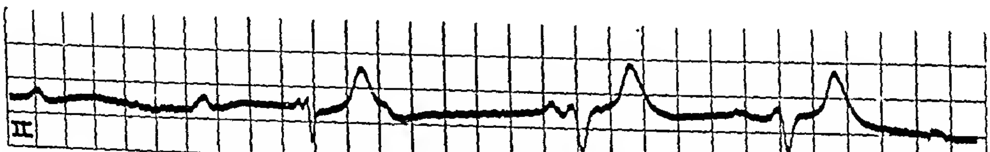


Fig. 14.—This record likewise shows only auricular complexes. Note the variation in the amplitude of the P-waves and the evident arrhythmia.

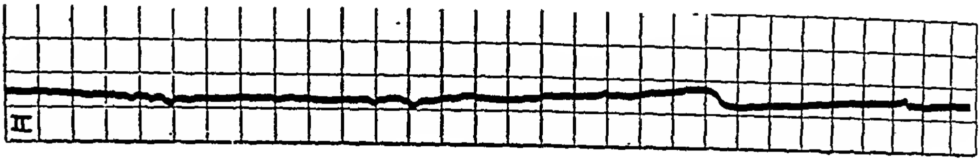
Fig. 15.—This record shows ventricular recovery. Note the change in direction of the ventricular complexes presumably indicating a shifting origin of the idioventricular rhythm.

The resumption of ventricular activity is shown in Fig. 15. The ventricular components are completely reversed but recovery took place.

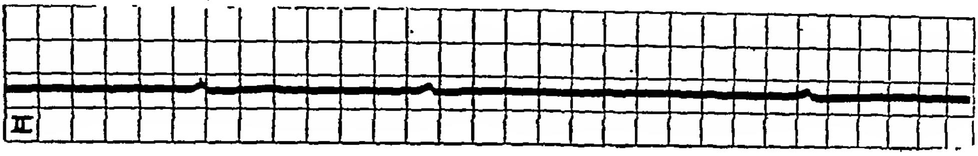
Figs. 16, 17 and 18 also show a period of high grade block with recovery.

Remarkably long periods of complete cardiac asystole are recorded in Figs. 19 to 24, and long periods of ventricular asystole with high grade block, in Figs. 25 and 26.

16.



17.



18.

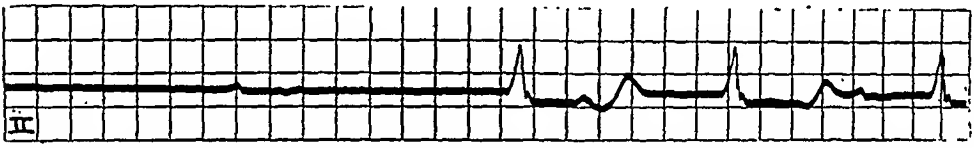
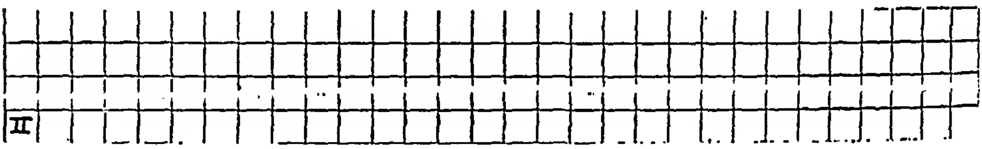


Fig. 16.—This record shows a long period of ventricular asystole with only occasional P-waves. Some of the first irregular undulations are probably artefacts.

Fig. 17.—This record shows continued ventricular asystole with only three auricular waves, occurring irregularly.

Fig. 18.—This record shows ventricular recovery.

19.



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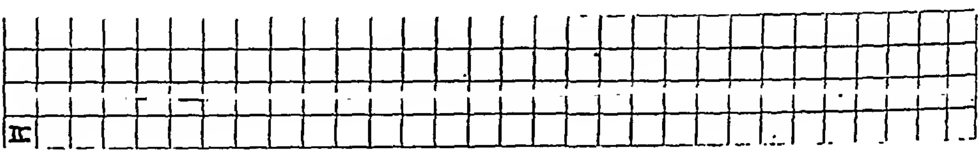

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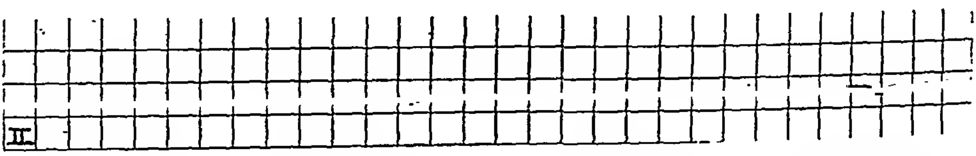

Fig. 19.—This record displays a remarkably long period of complete cardiac asystole.

Fig. 20.—This record is identical in character with the preceding one but successively continuous in time.

Fig. 21.—This record shows the continuation of complete cardiac asystole.

The high grade block exhibited at times in this case is not unlike that seen in the dying human heart. Under conditions of impending death,

when evidence of disease of the conduction paths has not been apparent, the appearance of varying degrees of block has been attributed to asphyxia. It is not unlikely, therefore, that some of the phenomena observed in this case were, in part at least, influenced by asphyxial states.

Fig. 22.

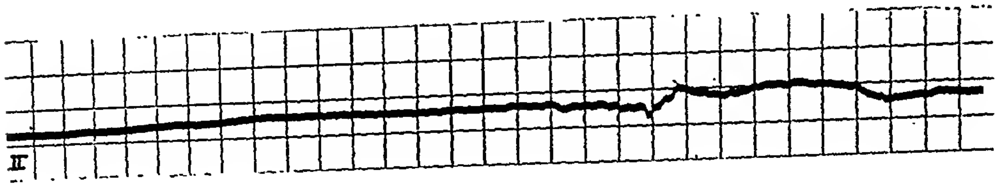

Fig. 23.

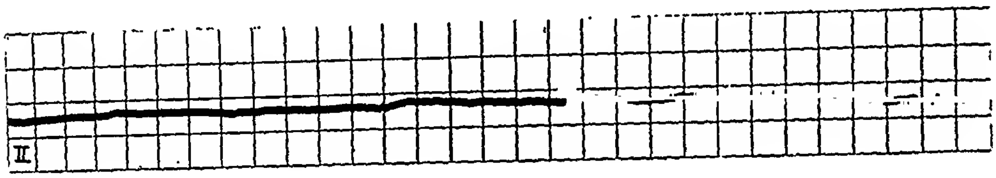

Fig. 24.

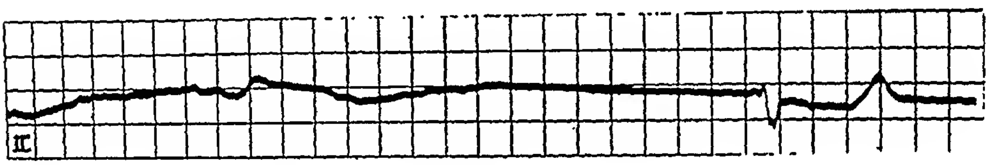

Fig. 22.—This record shows complete cardiac asystole and one peculiar deflection which may represent an attempt at ventricular activity.

Fig. 23.—This record shows complete cardiac asystole. The slight deflection shown appears to be an artefact.

Fig. 24.—This record shows temporary ventricular activity.

Fig. 25.

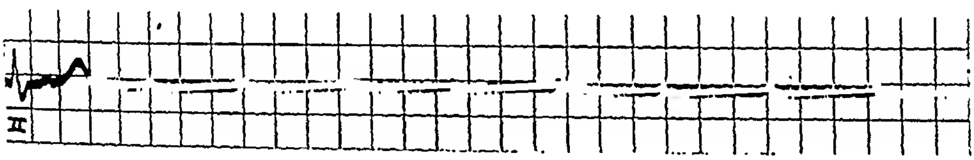

Fig. 26.

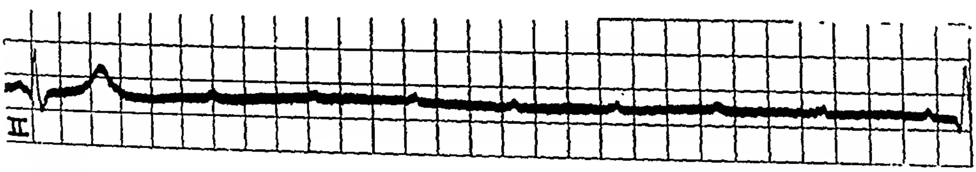

Fig. 25.—This record shows 10:1 block.

Fig. 26.—This record likewise shows high grade heart-block.

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THE DISTORTION OF THE ELECTROCARDIOGRAM BY ARTEFACTS*

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ARTEFACTS of various kinds are encountered in varying degrees in any large series of electrocardiograms, their number depending in part on the accuracy of the technic employed and in part on the types of idividuals electrocardiongraphed. To those of wider experience such artefacts are usually readily recognizable, but to those whose experience has been more limited, they are a frequent source of perplexity in the interpretation of the tracings. In a rather large percentage of the electrocardiograms that have been referred to this laboratory for an opinion, artefacts have been found responsible for the difficulties that have been met in their analysis. For this reason we believe that a brief account of our experiences with electrocardiographic artefacts may prove helpful. This experience we are summarizing in this paper.

The literature makes little mention of the distortion of the electrocardiogram by artefacts, although certain writers, in particular S. Calvin Smith,† have illustrated a number of them. Texts on electrocardiography, as a whole, devote very little space to the subject.

We have examined the 15,600 electrocardiograms‡ that have been taken in this laboratory during the past several years, and have selected those showing artefacts. These we have divided into several groups, depending upon their cause, and have chosen one of the most typical from each of the more important groups or subgroups for illustration.

Artefacts are usually about evenly divided between those of intrinsic origin, that is arising within the individual himself and those of extrinsic origin, that is, arising from instrumental factors outside of the body. These intrinsic and extrinsic factors are in turn divided into subgroups.

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*From the Cardiographic Laboratory of the Massachusetts General Hospital, Boston, Mass.

†Smith, S. Calvin: Heart Records, Their Interpretation and Preparation, 1923, F. A. Davis Co.

‡These electrocardiograms were taken with the string galvanometer manufactured by the Cambridge Scientific Instrument Company of Cambridge, England, in 1914. The observations in this paper refer to the string type of galvanometer but are also applicable in part to other types of galvanometers.

A. INTRINSIC FACTORS

The intrinsic factors are in the main due to somatic muscular activity.

1. *Muscular Contractions.*—When there is a single contraction or movement of a large skeletal muscle or group of such muscles, there is often a considerable effect produced upon the string of the galvanometer. Depending upon the movement various effects are recorded, from the raising of the base line to simulate a P- or T-wave or a QRS complex to the forcing of the string beyond the limits of the photographic field. In Figs. 1, 2, and 3 this condition is illustrated: as a single muscle movement in Fig. 1, as a recurrent facial, arm and shoulder tic in Fig. 2, and as the constant rapid distortion of paralysis agitans in Fig. 3. Strange as it may seem, these artefacts in unskilled hands are often the most difficult to interpret, since the individuals electrocardiographed have not been closely observed at the time for the detection of such abnormal muscle action, and unusual P-, QRS or T-waves have been thought present. The larger the muscle and the nearer to the electrodes, the greater is the distortion that results from its contraction.

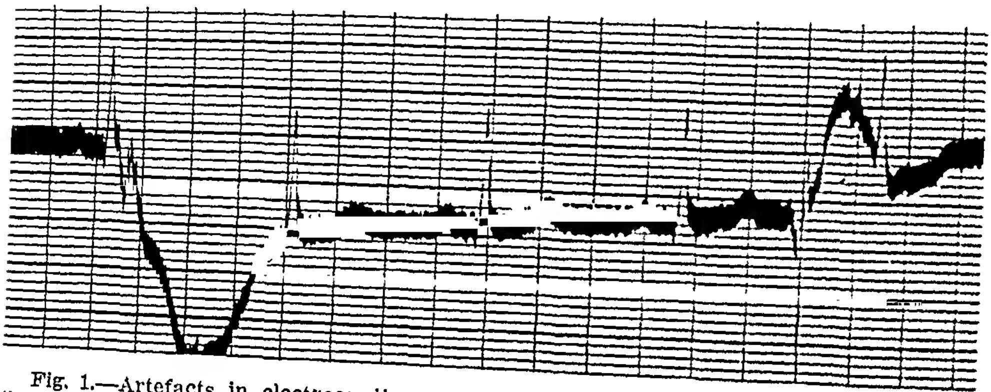

Fig. 1.—Artefacts in electrocardiogram (Lead I), consisting in a displacement of the base line due to muscle movement (contraction and movement of left hand and later of the right hand in electrodes). Times lines represent fifths of a second, amplitude is expressed in 10^{-4} volts in this and in the following figures.

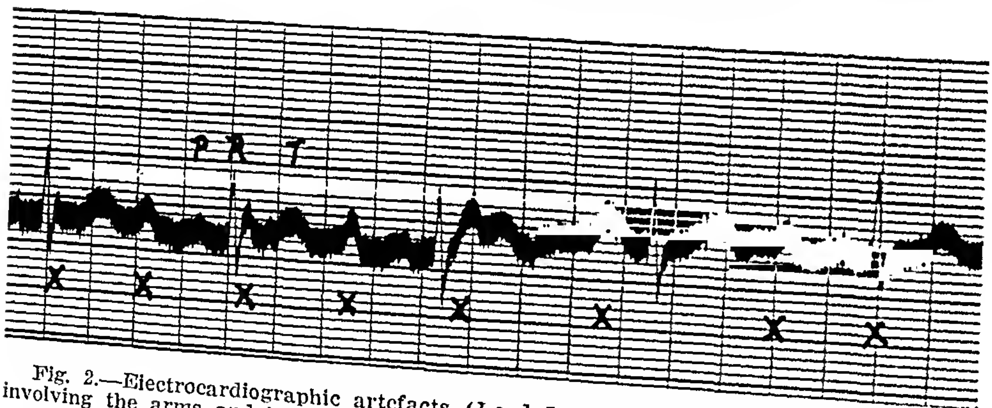

Fig. 2.—Electrocardiographic artefacts (Lead II) due to a regularly recurring tic involving the arms and head. The deflections due to the tic are marked by an x.

2. *Somatic Tremor.*—Undoubtedly the most frequent type of all artefacts is due to varying degrees of somatic or nervous tremor (Fig. 4).

This is the result of the fine rapid action of fibers in the somatic musculature from the tension of nervousness or hyperthyroidism or actual spastic contraction. It is at times present to an extent sufficient to mask the cardiac deflections.

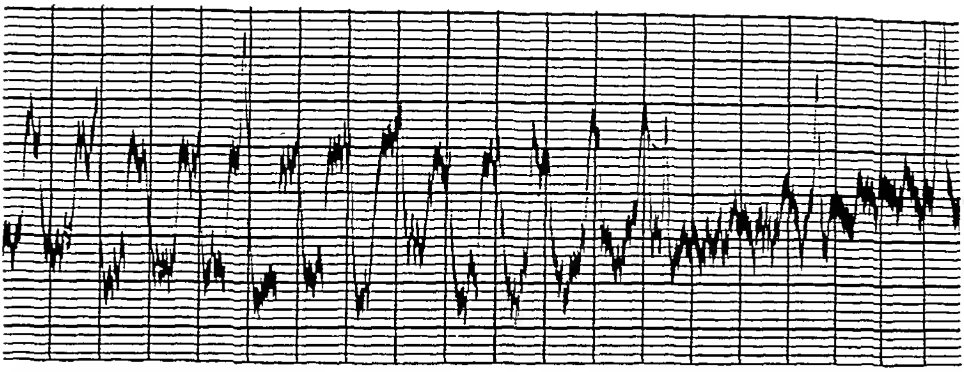

Fig. 3.—Artefacts due to paralysis agitans. The coarse skeletal muscular movements occurring about five times a second caused striking regular wide deflections of the base line, at times burying the auricular and ventricular deflections, but at other times the QRS group can be easily made out superimposed on the artefacts. At the end of the record auricular flutter is simulated.

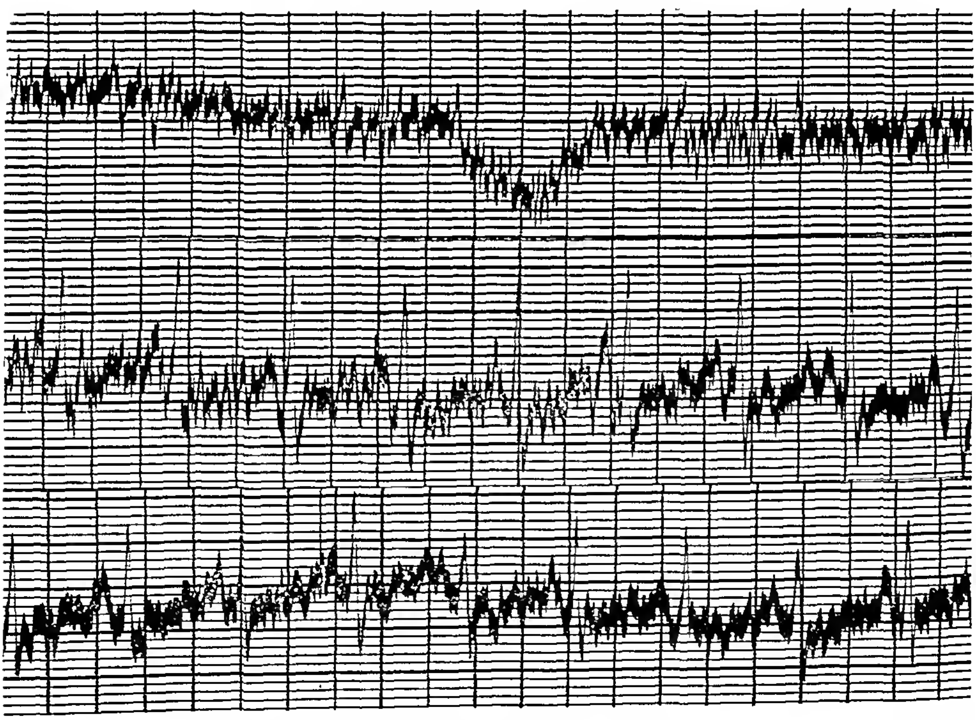

Fig. 4.—Electrocardiogram showing marked somatic or "nervous" tremor deforming all three leads. In Lead I it is particularly difficult to distinguish any deflections of cardiac origin.

3. *High Resistance With Loose String.*—In some cases in which the so-called skin resistance is high, the string of the galvanometer must be loosened excessively to allow proper standardization, a deflection of one centimeter for one millivolt. The degree of loosening may result in a marked deformation of the deflections, and sometimes in such

cases an overshooting of the string also occurs. This condition is not uncommon and an example is shown in Fig. 5. If marked, the deformity of QRS or T-waves may simulate some important pathological conditions, like intraventricular block or the abnormal T-wave of coronary disease. It should also be observed that high resistance (over 2000 ohms) frequently originates not in the individual, but in

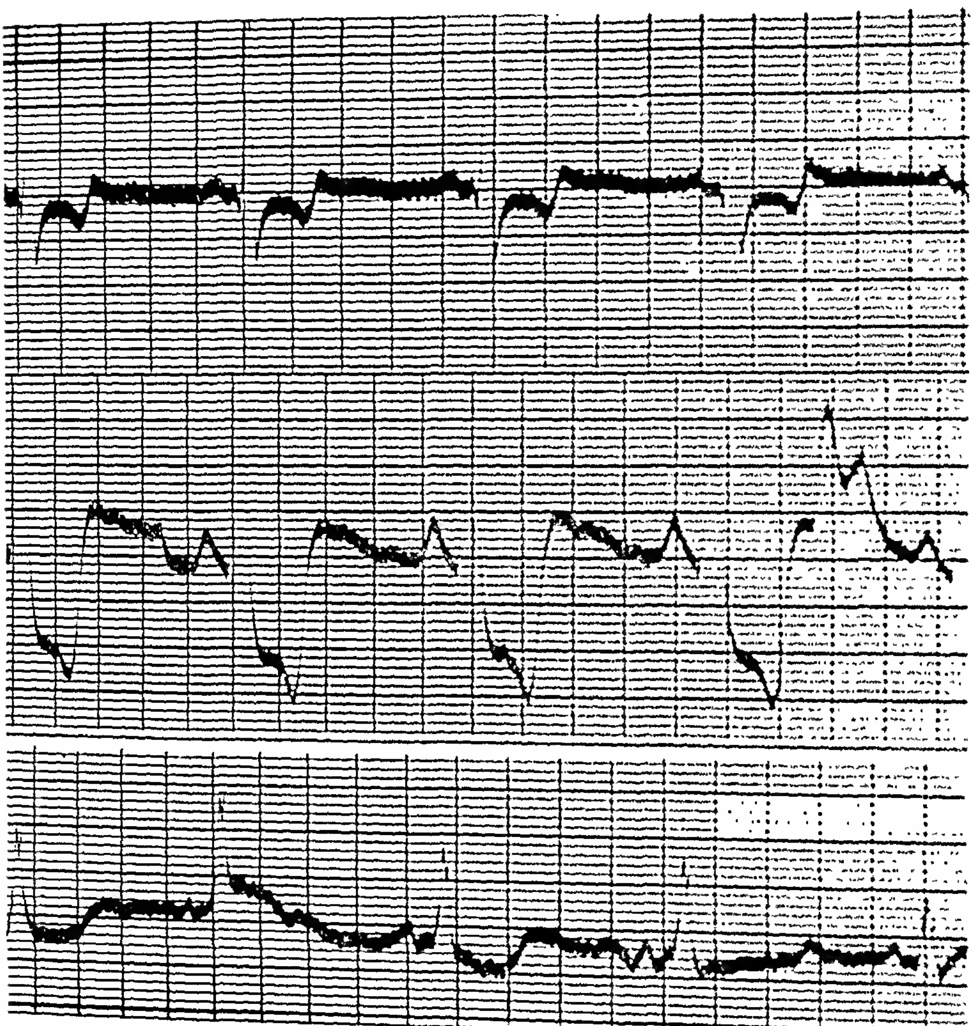

Fig. 5.—Electrocardiogram (Leads I, II, and III) showing artefacts due to high resistance and polarization. Also at the end of Lead II there is an artefact due to somatic muscle movement.

the instrumental connections, if for example the electrodes themselves are faulty, as when fresh water instead of salt water is used or when rust collects on the terminals, especially in humid weather.

B. EXTRINSIC FACTORS

1. *Polarization of Electrodes.*—As Einthoven, Lewis, Pardee, and others have pointed out, polarization of electrodes may cause important artefacts, chiefly shown by overshooting of the string and a movement back to or beyond the base line even when a constant current

is maintained. This neutralizing or exaggerating effect of polarity is largely avoided by the use of nonpolarizable electrodes, but for practical purposes polarizable electrodes may be employed, with only oc-

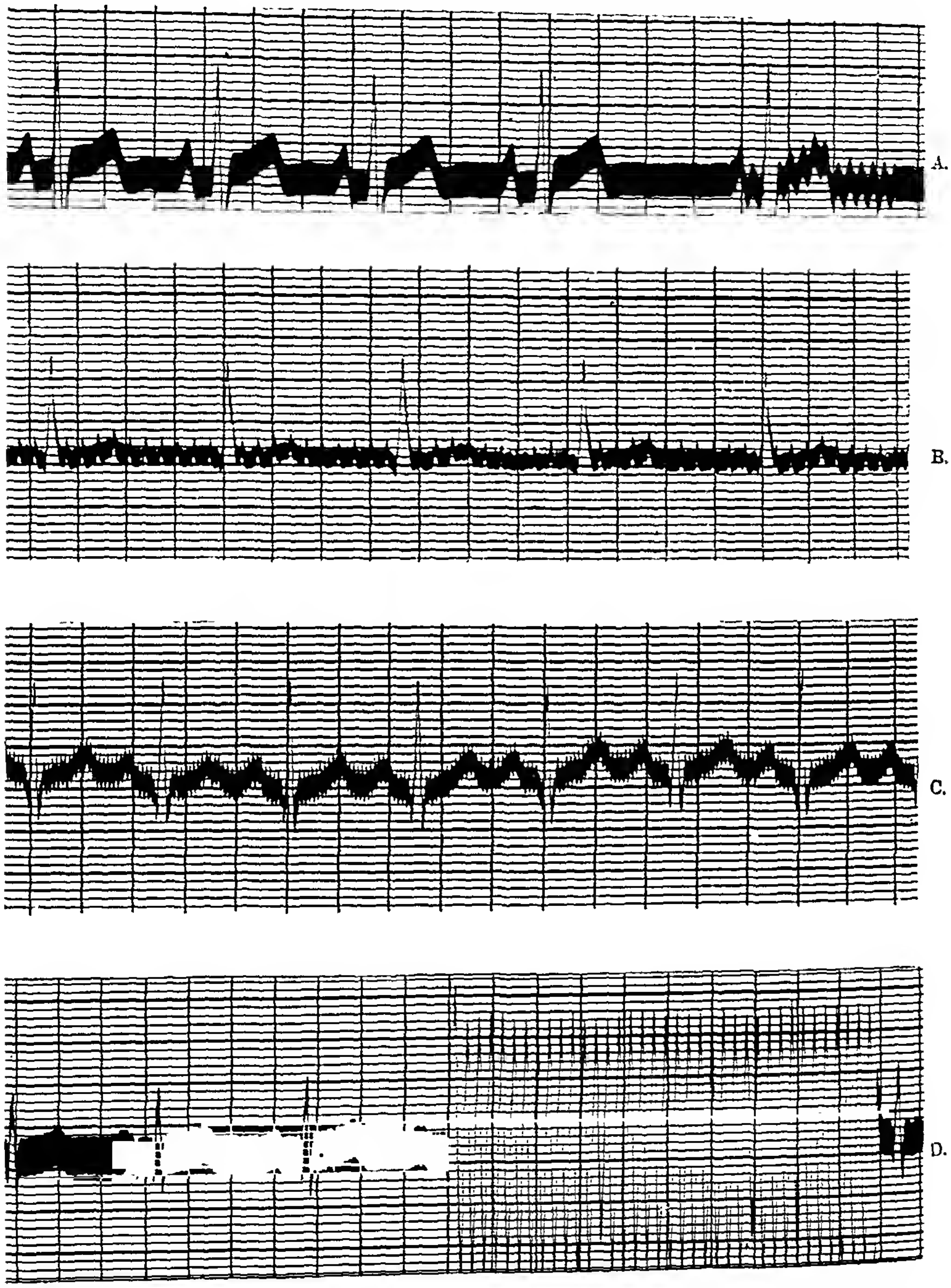

Fig. 6.—Electrocardiograms (*A*, *B*, *C*, and *D*) illustrating various rhythmic disturbances of the base line due to induction from outside currents at varying rates and strength. *A* and *D* represent short intervals of artefact due to the ringing of a telephone bell. *B* and *C* represent constantly recurring distortions, at a cycle of 15 per second in *B* and of 60 per second in *C*.

casional distortion of the electrocardiogram, provided the surface contacts between patient and electrodes are large. Nevertheless it is important always to be on guard against the artefacts due to polariza-

tion in using polarizable electrodes. Fig. 5 illustrates this artefact as well as that resulting from too high a resistance.

In addition to the high resistance and polarization of the electrodes there are a number of other important extrinsic causes of artefacts.

2. *Outside Current (Induction).*—In Fig. 6 is illustrated a type of artefact occurring much more frequently in the past than at present when electrocardiographic equipments are better constructed and protected. It is produced by the effect on the string of an outside current, for instance from a ringing telephone or an adjacent x-ray machine. A series of regular waves is produced, at times so marked as to be easily recognized, but in some instances more confusing because only the base line may appear to be affected. Four types of varying rate and amplitude are illustrated in Fig. 6.

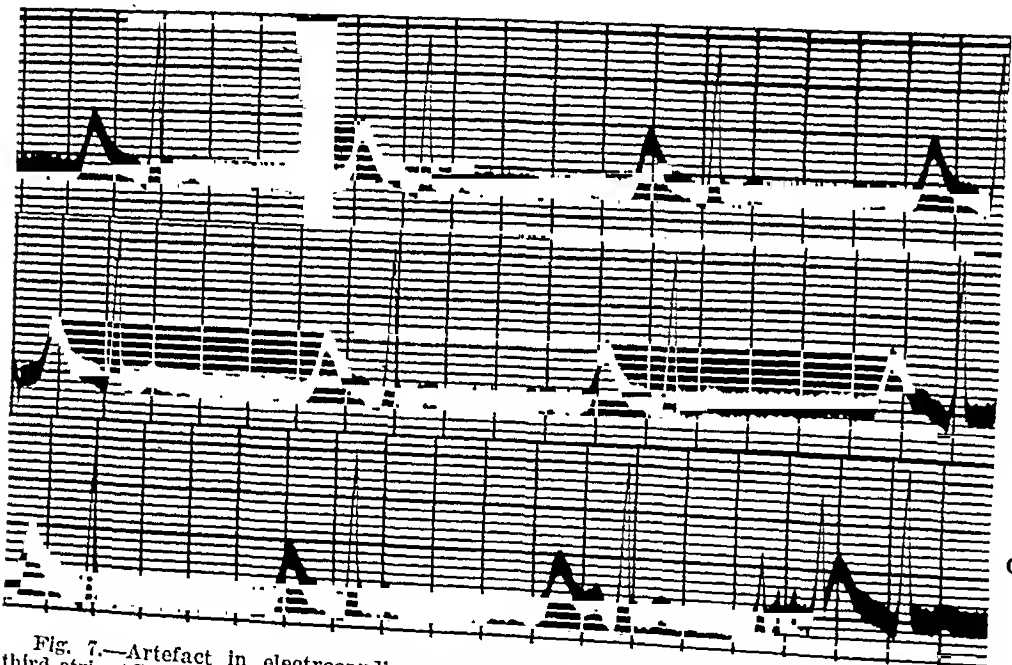

Fig. 7.—Artefact in electrocardiogram due to faulty contact shown near end of third strip (*C*). The plate was wrongly placed in the camera with the film side away from the light resulting in reversion of record when printed in routine way. The second thus reads from right to left. Also a black band is seen in *A*, due to flickering of the arc light.

3. *Faulty Contacts.*—Another type of artefact is that caused by a switch defect, commonly in the Wheatstone bridge of the electrocardiograph. Loose or dirty contacts are usually responsible. In this case the tracing shows a series of uneven and irregular lines interrupting the cardiac deflections for usually not more than a few fifths of a second. An example of this is shown in Fig. 7. This illustration also shows faulty technic in photography. The plate was reversed end for end with the result that all leads read from right to left. We have known instances of the incorrect interpretation of the P-wave as the T and the T-wave as the P when this reversion has occurred.

4. *Reversed Electrodes.*—If the lead wires are not properly applied, a confusing picture may be produced.* Thus in Fig. 8, in which this error has been made, it will be seen that a reversion of the leads explains the difficulty. The wires attached to the terminals of the right arm and left arm have been reversed, resulting in Lead I being recorded upside down, Lead III being recorded in the place of Lead II, and Lead II recorded in the place of Lead III.

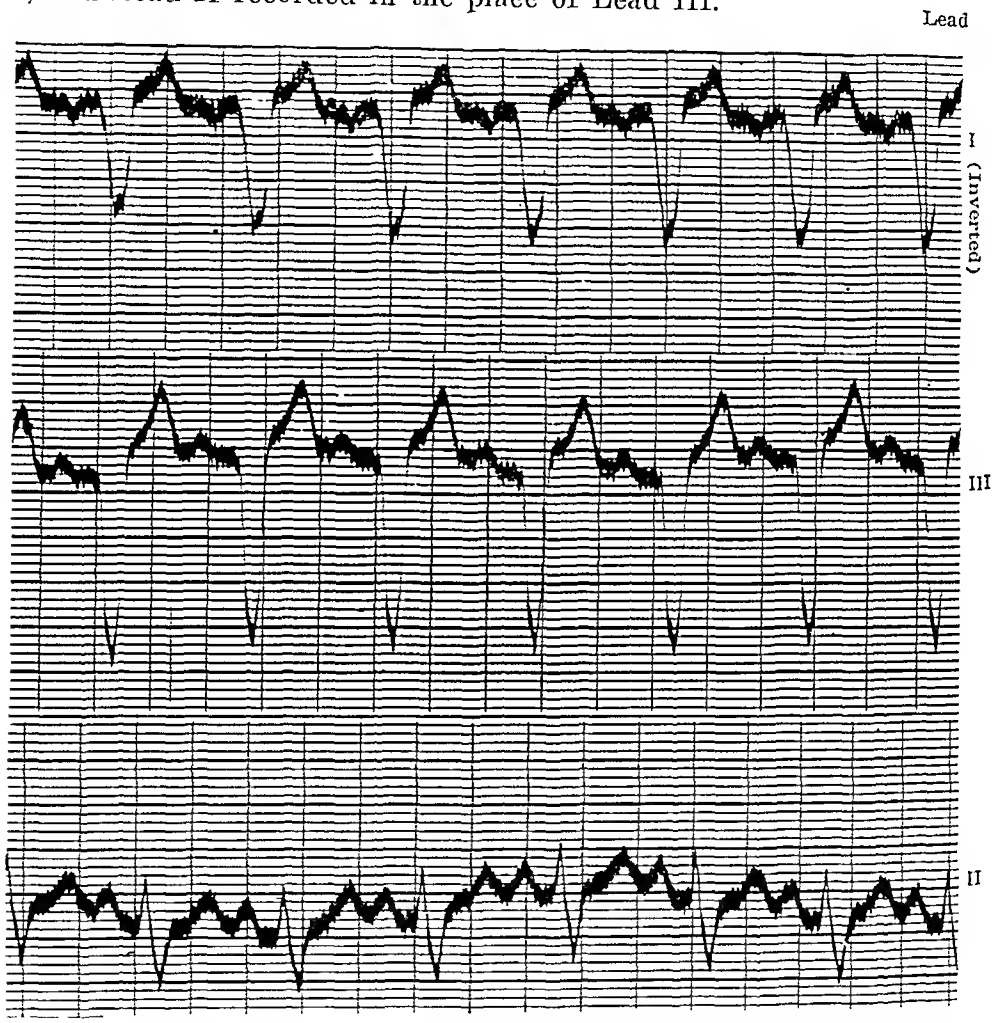

Fig. 8.—Artefact in electrocardiogram due to crossing of leads. The right and left arm wires were wrongly attached (reversed), resulting in inversion of Lead I and transposition of Leads II and III. Right bundle-branch block is present, but at first glance in the uncorrected record the interpretation appears confusing. The inversion of P in Lead I helps to reveal the error.

5. *Composite Electrocardiograms.*—Fig. 9 illustrates a double electrocardiogram. The leads were applied to a child who was held by the mother in her lap during the taking of the tracing. As will be seen the mother's heartbeat is recorded along with that of the child.

In addition to these artefacts there may occur a few others. At times at the beginning of a tracing the time marking wheel, if such is

*Error in the wiring of wards by electricians may result in this same artefact even though the electrodes themselves appear properly applied.

used, may be started at too rapid a rate and may continue to revolve at double speed throughout the tracing. Thus the time lines will separate tenths of a second instead of the customary fifths. Again in those instruments in which plates are used and the speed of the plate is controlled by an oil chamber, if an air bubble gets into the oil when the cylinder is not sufficiently filled, the plate will move faster than its accustomed rate for a short interval, resulting in the widening of the time markings and a distortion of the tracing. A further distortion of the electrocardiogram may come from irregular movement of plate, or roll of paper or film, in the camera due to incorrect working of the mechanism. This, of course, can almost always be easily detected.*

Artefacts due to inexact standardization are, of course, not recognizable in themselves on inspection of the electrocardiogram but comparison of several records from the same patient, perhaps taken on different occasions, will reveal this error. Naturally one assumes that

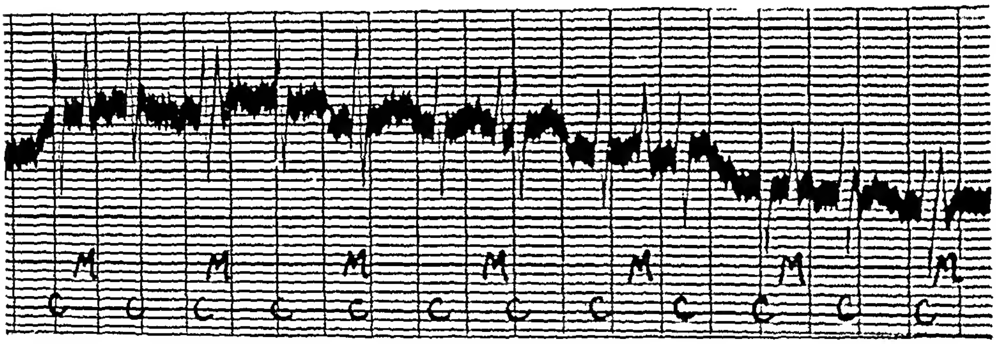

Fig. 9.—Artefact due to composite electrocardiograms of Lead I of infant and of mother who held the baby's arms with her own hands. The child's ventricular complexes are marked *C* and the mother's *M*. The auricular deflections are not evident. The infant's heart rate was 180 per minute and the mother's 100.

this type of artefact is routinely guarded against at the time the electrocardiogram is taken.

Of course there may also arise errors in photography, recording, and filing, but these are simple and quickly recognized and need not concern us further.

SUMMARY

The frequency with which the electrocardiogram may be distorted by artefacts, especially since the widespread use of the galvanometer in clinical work, demands more consideration than is usually accorded it.

We have presented a brief discussion of the more important of these artefacts that have come to our notice in the past thirteen years, and have divided them into two groups, as they may be intrinsic or extrinsic in origin. Illustrations of the more important artefacts have been added.

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*If an arc light is used, flickering or sputtering due to carbon impurities or to faulty adjustment may streak the record.

Artefacts of intrinsic nature may arise from single contractions or movements of skeletal muscles, from repeated contractions of such muscles, as in a tic, from paralysis agitans, and finally from the tension of muscles constantly in contraction (called somatic tremor), as in nervous or hyperthyroid individuals. The high resistance of the subject or of the instrument itself may also give rise to artefacts due to the inertia of a loosened string.

Artefacts of extrinsic origin include those due to high resistance, polarization of electrodes, outside current, faulty contacts, reversed leads, composite electrocardiograms, and errors in photography or in the manipulation of the time marker.

HEART MURMURS: THEIR INCIDENCE AND INTERPRETATION

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Columbia, S. C.

LAENNEC'S experience with heart murmurs may be said to typify the confusion and uncertainty that have surrounded this subject since the great Frenchman devised the stethoscope and made it possible for us to hear the sounds that are generated over the precordium. It is said that in the beginning he looked upon all of the murmurs that he heard as indicative of disease of the cardiac valves. But after following many of the patients in whom he had heard such murmurs to the autopsy table, and finding no anatomical confirmation of his antemortem impressions, he concluded that murmurs over the heart were entirely without significance.[1] We know now that both of his conclusions were wrong; that some of the murmurs are indicative of defects in cardiac structure; that many of them point to no such defects, and that careful examination and discriminating judgment will enable us properly to differentiate them.

In my work as a consulting physician I became impressed with the frequency with which innocent murmurs over the precordium were interpreted as indicative of cardiac pathology, and the patients reduced to the unhappy state of cardiac neurasthenics. This unfortunate state of affairs was not infrequently encountered after routine examinations for life insurance, healthy applicants leaving the examiners' hands with their attention attracted to their hearts for the first time, and with a fear of heart disease fixed upon them. Other patients were seen who had been advised of these murmurs following examinations that had been made in the course of trivial illnesses, and who had had unnecessary physical restrictions placed upon them because of the assumption that the murmurs demanded protection of the heart muscle.

It occurred to me that it might prove interesting and serviceable to collect data concerning the incidence and significance of murmurs heard over the precordium in the course of routine office examinations. With this idea in mind, I paid especial attention to all such murmurs in a series of 1166 consecutive cases.

In doing this work I adopted the following classification of heart murmurs:

I. *Organic Murmurs.*—Under this heading were listed all murmurs that were interpreted as indicative of organic change in the structure

of the heart valves, those engendered by a disease of the aortic arch, and those indicating a persistence of embryonic openings between the chambers of the heart or a persistent ductus botalli.

II. *Accidental Murmurs.*—Under this broad heading were classed all murmurs which were interpreted as being without significance of organic change in the structure of the heart valves, and not dependent upon any form of congenital heart disease or abnormality in the aortic arch. These murmurs were subdivided as follows:

1. Intracardiac accidental murmurs.
2. Extracardiac accidental murmurs.

The intracardiac accidental murmurs were looked upon as those which probably found their origin inside of the heart as the result of a dilatation of the valvular rings (inorganic murmurs), because of a change in the quality of the blood (hemic murmurs), or because of a deformitory of a valvular orifice produced by a displacement of the heart, as in pleural effusion. The extracardiac murmurs were regarded as arising outside of the heart and were clearly demonstrated to be dependent upon some phase of respiration. Under this head one murmur was designated as pleuropericardial because of its superficial, scratchy character and its persistence in all phases of respiration.

The criteria for the grouping of the murmurs were as follows:

1. A careful history, with emphasis on the past or present occurrence of cyanosis, dyspnea and edema, the rheumatic triad, and syphilis.

2. The time and quality of the murmur and its transmission, if any.

3. The association of the murmur with thrills, accentuation of the second sounds, and the height of the systolic and diastolic arterial pressures.

4. The presence or absence of anemia.

5. The presence or absence of cardiac hypertrophy as determined by percussion and roentgenographic study.

TABLE I

		PER CENT
Total number of cases examined	1166	
Murmurs heard in	166	14.2
Accidental murmurs	127	10.9
Organic murmurs	39	3.3
Mitral insufficiency	15	1.3
Mitral stenosis	8	0.7
Aortic insufficiency	10	0.8
Dilated aorta (3) Aneurysm (1)	4	0.3
Congenital heart lesion	2	0.2

It will be noted from Table I that accidental murmurs were heard in 10.9 per cent of the patients examined. Potain,[2] the great French cardiologist, reported an incidence of such murmurs in 12.5 per cent of all of the patients seen in his hospital service. He found them with especial frequency in association with exophthalmic goiter, chlorosis, and the acute fevers. Thayer[3] reported murmurs of this type in 56.4 per cent of patients in the first decade of life, with a gradually diminishing incidence according to decades up to the fourth where he found murmurs in 19.2 per cent. These figures certainly tend to emphasize the importance of the subject.

TABLE II

		PER CENT
Total number of murmurs	166	
Accidental murmurs	127	75.6
Mitral insufficiency	15	9.0
Mitral stenosis	8	5.0
(Total mitral murmurs	23	13.9)
Aortic insufficiency	10	6.0
Dilated aorta or aneurysm	4	2.3
Congenital heart lesions	2	1.2

In Table II we see that 75 per cent of the murmurs heard over the precordium in this series are of no pathological significance. This should serve to emphasize the very great care that should be exercised before a murmur is interpreted as indicative of a cardiac lesion.

TABLE III

SEX INCIDENCE

	NUMBER	PER CENT
Males	46	37
Females	81	63

In this series accidental heart murmurs were heard almost twice as frequently in females as in males. Of the 1166 patients examined, 549 were males and 617 females. Thus, the indications are that accidental murmurs are to be expected with much greater frequency in the females.

TABLE IV

INCIDENCE OF ACCIDENTAL MURMURS ACCORDING TO DECADES

DECADE	MURMURS	PER CENT	NO. OF PATIENTS	PER CENT
First	3	2.5	27	11.0
Second	11	8.6	103	10.7
Third	43	33.0	269	16.0
Fourth	33	26.0	265	12.5
Fifth	21	16.0	207	10.0
Sixth	10	.8.0	154	6.5
Seventh	5	4.0	110	4.5
Eighth	1	0.5	31	3.2

The figures in Table IV show both a relative and an absolute maximum incidence of accidental murmurs in the third decade; but it seems to me that the most important showing of all is that these murmurs may be encountered in any decade of life, and that we should be ever on guard to interpret them properly.

TABLE V

SITE AT WHICH ACCIDENTAL MURMURS ARE BEST HEARD

	NUMBER	PER CENT
At the base of the heart	61	48
At the apex of the heart	28	23
Audible at apex and base	99	78
Equally at apex and base	34	26
Audible at aortic area	6	4
Total heard at base	107	84

Table V serves to stress the importance of the well recognized fact that accidental murmurs are most often heard at the base of the heart. In only 16 per cent of the cases were the accidental murmurs heard at the apex alone. It might be said with propriety that a systolic murmur at the base of the heart should be considered innocent until proved otherwise.

TABLE VI

TIME AND QUALITY OF ACCIDENTAL MURMURS

	NUMBER	PER CENT
Systolic	127	100
Diastolic	0	0.0
Soft	88	70.0
Loud	35	27.0
Musical	17	13.0
Superficial	10	8.0
Scratchy	1	0.8

Table VI shows that all of the accidental murmurs were systolic in time. Diastolic murmurs of this type are said to occur,[4] but I failed to find a single instance in this series. The great majority of these murmurs are classed as soft, but the loud, musical, and superficial ones are sufficiently numerous to keep us from generalizing as to the significance of these qualities. It is well known that the qualities of murmurs that are found in association with organic valvular disease vary tremendously and have little significance, especially as regards loudness and softness, or more properly, the intensity of the murmur, and this seems to apply equally well to the accidental murmurs. I should say that the quality of a murmur is no criterion for decision as to its accidental or pathological generation.

It is well known that in contrast with organic murmurs the accidental ones are not well transmitted in any direction. Of the 12 accidental murmurs in this series that were transmitted toward the axilla

TABLE VII

TRANSMISSION OF ACCIDENTAL MURMURS

	NUMBER	PER CENT
To axilla from apex	12	9.4
Upward from the base	1	0.8

from the apex, 10 of them were of the cardiorespiratory type with the murmur definitely dependent upon a phase of respiration, 1 of them was classed as a hemic blow in association with a hemoglobin of 68 per cent, and 1 as an inorganic murmur in connection with cardiac hypertrophy and dilatation resulting from a long-standing hypertension, the patient having a systolic pressure of 180 mm. and a diastolic pressure of 120 mm. The murmur which was transmitted upward from the base was regarded as an inorganic one due to relative narrowing of the aortic ring in association with a pronounced hypertension.

The pulmonic second sound was found to be accentuated in 5 instances, or 4 per cent of the cases, in which accidental murmurs were heard. Three of these patients showed relatively insufficient myocardial function in connection with hypertension, adiposity, or both, and one was found in association with a pleural effusion. In all of these cases sufficient cause was found to account for an increased pressure in the pulmonary circulation without the existence of an organic valvular insufficiency. In one case no explanation could be offered for the accentuated second sound. These figures serve to emphasize the importance of an unaccentuated second pulmonic sound in establishing the innocence of precordial systolic murmurs.

TABLE VIII

ENLARGEMENT OF HEART AND AORTIC DILATATION IN ASSOCIATION WITH ACCIDENTAL MURMURS

	NUMBER	PER CENT
Cardiac hypertrophy	11	8.6
Aortic dilatation	5	4.0

In the interpretation of cardiac murmurs it may be accepted as an axiom that an insufficient valve must result in an increase in the size of the heart. The only exception to this rule is in acute valvular disease where the insufficiency of the valve has not lasted long enough for the added demands upon the myocardium to produce hypertrophy of the heart muscle; however, cardiac hypertrophy may be found in association with accidental murmurs as well. This series shows such hypertrophy in 11 instances, or in 8.6 per cent of the murmurs recorded as accidental. In 8 of these cases the hypertrophy was ascribed to pronounced systemic hypertension; in one to a severe ane-

mia;[4] in 1 to extreme adiposity, and in 1 to a long neglected pleural effusion. Hypertension was regarded as the explanation of all of the instances of aortic dilatation. In other words, an adequate cause, other than an organic disease of the heart valves, was present to account for the enlargement of the heart or the aorta in all the cases so grouped.

TABLE IX

CLASSIFICATION OF ACCIDENTAL MURMURS

	NUMBER	PER CENT
Intracardiac	36	28.3
Inorganic	12	9.4
Hemic	21	16.0
Cardiac displacement	3	2.3
Extracardiac	91	71.7
Cardiorespiratory	90	70.9
Pleuropericardial	1	0.8

Table IX shows the great preponderance of cardiorespiratory murmurs over accidental murmurs of other types. It is fortunate that this type of murmur is the most easily differentiated from murmurs arising from valvular heart disease. These murmurs can be clearly related to the juxtaposition of the heart and lung, disappearing on some phase of respiration, being more clearly heard at the base than at the apex, and tending to diminish in intensity or disappear with the patient in the upright position. The so-called hemic murmurs should likewise give rise to little confusion when their association with more or less pronounced anemia is kept in mind. The inorganic type of accidental murmur requires more careful differential study for its recognition, and its practical importance as an accidental murmur is not so great, as it is truly indicative of cardiac embarrassment and must be looked upon as significant.

TABLE X

RELATIONSHIP OF ACCIDENTAL MURMURS TO BODY WEIGHT

	NUMBER	PER CENT
Underweight	84	66.0
Normal weight	21	16.0
Overweight	22	17.0

As would be expected, accidental murmurs are most frequently heard in patients who are below their optimum weight, for the asthenic type of person, with the long and narrow chest, has the left border of the heart and the anterior lappet of the left lung in close apposition. These are optimum conditions for the generation of cardiorespiratory murmurs; but it is important to remember that such murmurs are to be heard also in patients who are at or above their proper weights.

TABLE XI

BLOOD PRESSURE, PULSE AND HEMOGLOBIN

	NUMBER	PER CENT
Blood pressure		
Below 111 mm. systolic	45	35.0
Above 130 mm. systolic	30	23.0
Normal	52	41.0
Pulse		
70 to 90	65	51.0
Below 70	9	7.0
Above 90	53	41.0
Hemoglobin		
Below 75 per cent	41	32.0
Above 74 per cent	86	67.0

The blood pressure and pulse rate seem to be practically unrelated to the incidence of accidental heart murmurs. The exception to this statement is in the fact that long-standing hypertension brings about changes in the heart and aorta that produce murmurs of the inorganic variety. Accidental murmurs are not heard with any greater frequency in association with hypotension than they are in patients with normal blood pressure. The pulse rate was within normal limits in 51 per cent of the cases. In the presence of pronounced anemia we naturally expect to find "hemic blows" over the precordium, but these statistics show that 67 per cent of the patients with accidental murmurs had no anemia.

In 6 of these patients with accidental heart murmurs, or 4.7 per cent, a diagnosis of organic heart disease had been made on the basis of the murmur alone. In all of these cases the murmurs were of the cardiorespiratory type, and the mistake should have been easily avoided.

CONCLUSIONS

1. In 1166 patients 127 accidental heart murmurs were discovered, while 39, or 3.3 per cent of them, showed murmurs indicative of organic valvular disease.

2. All of the accidental murmurs were systolic in time, and 84 per cent of them were heard at the base of the heart.

3. Transmission of accidental murmurs is relatively rare. Nine and four-tenths per cent of the murmurs so classified were transmitted to the axilla, and only 0.8 per cent upward from the base. Cardiac hypertrophy was encountered in association with accidental murmurs in 8.6 per cent of the cases, but in every instance it was possible to account for the hypertrophy independently of the murmur. Cardiac hypertrophy is a necesary part of organic valvular disease.

4. Accentuation of the pulmonic second sound is heard in connection with accidental murmurs of the inorganic type, but is not to be expected with other types of these murmurs.

5. Other evidence than that afforded by a murmur must be found before a heart is assumed to be diseased.

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STATISTICAL STUDIES BEARING ON PROBLEMS IN THE CLASSIFICATION OF HEART DISEASES

V. Heart Disease Among Ex-Service Men*†

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INTRODUCTION

THIS study was undertaken to ascertain the varieties of heart disease found among ex-service men; to classify these by etiology, structural lesion and functional capacity; and to attempt to analyze the cardiovascular findings in a group of men under hospitalization in the U. S. Veterans Bureau. While the average age of the World War veteran is approximately thirty-five, there are a considerable number of veterans of the Spanish American War, Philippine Insurrection, and other campaigns with an average age of fifty-four; the average age of all veterans is approximately thirty-six.

The data compiled and analyzed in this study were obtained by means of a questionnaire, which was issued to all of the U. S. Veterans hospitals and was executed on all of the Bureau beneficiaries under hospitalization for heart disease during 1926. The number of beneficiaries was 736.

These patients were under treatment in some 53 hospitals, and their cardiovascular diseases were studied and diagnoses made by Bureau physicians, some of whom have had no special training in heart disease. It would seem, therefore, that there might be a lack of uniformity in diagnostic criteria and in the diagnosis of heart disease. As the result of this it is possible that the classification of the heart lesions is not uniform, so that the data compiled herein may not be as valuable as if collected at a well-organized heart clinic.

It is thought, however, that these data on heart disease serve their purpose in that they constitute a composite study of this class of disease in a select group of individuals under hospitalization. The work having been done by a number of Bureau physicians has resulted in the absence of any inclinations toward certain personal diagnostic tendencies.

Much stress has been laid by a number of writers[1, 2] upon the age of forty years as a period of the human life span when heart disease morbidity as well as mortality begins to mount. A study of heart

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disease at this time might contribute clinical as well as statistical information which would prove of value in any preventive measures in contemplation.

Dublin[2] states that five-sixths of the deaths from heart disease occur after the age of forty years, most of these being due to degenerative diseases and also arteriosclerosis. Cohn[1] contends that these deaths are not due to any definite disease processes, but, for the most part, to senescent changes of the heart and also to the fact that these subjects have been spared from earlier deaths resulting from infectious diseases and have succumbed to degenerative heart lesions.

As the result of this, Cohn, in a study of death rates by age groups, found a decided increase in the mortality rate from heart disease after the age of forty years. Under this age the death rate from heart disease has actually fallen.

INCIDENCE OF HEART LESIONS

Table I lists 1123 heart lesions found in 736 patients. The average number of lesions per patient is 1.53. It is noted that mitral insufficiency is the most common heart lesion recorded, followed by chronic fibrous myocarditis, hypertrophy of the heart, and aortic insufficiency, in the order named.

TABLE I

INCIDENCE OF HEART LESIONS IN A GROUP OF 736 EX-SERVICE MEN UNDER HOSPITALIZATION IN THE U. S. VETERANS BUREAU FOR HEART DISEASE

HEART LESION	NUMBER	PER CENT
Mitral insufficiency	301	26.80
Myocarditis, chronic, fibrous	153	13.62
Hypertrophy of heart	148	13.18
Aortic insufficiency	111	9.88
Mitral stenosis	65	5.79
Arteriosclerosis, general	50	4.45
Enlargement of heart	41	3.65
Aortitis without dilatation	35	3.12
Hypertension	26	2.32
Arrhythmia	25	2.23
Endocarditis, chronic	21	1.87
Aortitis with dilatation	18	1.60
Neurocirculatory asthenia	17	1.51
Auricular fibrillation	17	1.51
Tachycardia	10	0.89
Adherent pericardium	9	0.80
Arteriosclerosis, local	8	0.71
Myocarditis, acute	7	0.62
Aortic stenosis	6	0.53
Endocarditis, acute	5	0.45
Pericarditis with effusion	4	0.36
Atrophy of heart	2	0.18
Pulmonary stenosis	2	0.18
Hydropericardium	2	0.18
Heart-block	2	0.18
Tumor of pericardium	1	0.09
Pericarditis, fibrinous	1	0.09
Other lesions	36	3.21
Total	1123	100.00

Reference to this table indicates that general arteriosclerosis occurred 50 times and constituted 4.45 per cent of the total lesions under observation. This is of interest in view of the fact that the average age of the Veterans Bureau beneficiaries at the time this study was made was thirty-six years.

ASSOCIATED CARDIOVASCULAR LESIONS

Table II is so arranged as to indicate the principal as well as one associated heart lesion. In this connection it is desirable to state that in a number of cases there was more than one associated heart lesion, but that it was possible to tabulate only one with the principal diagnosis.

In reviewing this table it is noted that 453 patients had but one cardiovascular lesion. The table also attempts to illustrate the incidence of some of the principal cardiac lesions, as well as their combinations.*

Dublin,[2] quoting Wyckoff and associates in the study of 1000 cases of organic heart disease, found that a number of the patients had two or more lesions. Of the total lesions observed, enlargement of the heart was found 884 times in association with other lesions and 203 times alone; mitral insufficiency 495 times; mitral stenosis 443 times; aortic insufficiency 146 times; aortic stenosis 29 times; aortitis 169 times; mitral insufficiency and mitral stenosis 421 times; mitral insufficiency, mitral stenosis, and aortic insufficiency 162 times; and mitral insufficiency, mitral stenosis, aortic insufficiency, and aortic stenosis 12 times.

Associated Cardiovascular Lesions With Mitral Insufficiency.—Table III is a list of 301 cases of mitral insufficiency so arranged as to indicate the associated cardiovascular lesions. It is noted that 167 of these cases had no coexisting lesion; 77 had but one coexisting lesion; the remaining 57 cases had 2 coexisting lesions associated with mitral insufficiency.† The largest group was a combination of mitral insufficiency, aortic insufficiency, and hypertrophy of the heart. It is therefore seen that mitral insufficiency and aortic insufficiency frequently coexist in the same patient.

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*In determining the combinations of heart lesions in Table II it is first necessary to add the total number of lesions of each specific diagnosis found in the last column on the right to the total number of lesions of the same diagnosis at the bottom of the table: then subtract from this number the figure in the next to the last column, the latter indicating the number of times the particular heart lesion exists alone. The result of the above calculation is the number of times a particular lesion appears in combination. If it is desired to ascertain the number of times a lesion appears alone, the figures in the next to the last column only should be used.

†In determining the combinations of two coexisting heart lesions with the major diagnosis in Tables III, IV, V and VI, it is necessary to add the total number of lesions of each specific diagnosis found in the last column on the right to the total number of lesions of the same diagnosis at the bottom of the table; then subtract from this number the figure in the third column from the right, the latter indicating the number of times the particular heart lesion exists with but one coexisting lesion. If it is desired to ascertain the number of times a cardiovascular disease appears with one associated lesion, the figure in the third column from the right only should be used. It should be noted also that the figure in the second column from the right indicates the number of times a cardiovascular lesion appears alone.

TABLE II

CARDIOVASCULAR LESIONS IN 736 EX-SERVICE MEN UNDER HOSPITALIZATION IN THE U. S. VETERANS BUREAU FOR HEART DISEASE, INDICATING THE PRINCIPAL AS WELL AS ONE OF THE ASSOCIATED HEART LESIONS

CARDIOVASCULAR DISEASE	CARDIOVASCULAR DISEASE																										
	CARDIAC VALVULAR DISEASE MITRAL INSUFFICIENCY	HYPERTROPHY OF HEART	CARDIAC VALVULAR DISEASE, MITRAL STENOSIS	MYOCARDITIS, CHRONIC	CARDIAC VALVULAR DISEASE, AORTIC INSUFFICIENCY	ARTERIOSCLEROSIS, GENERAL	AORTITIS, WITHOUT DILATATION	AURICULAR FIBRILLATION	ARRHYTHMIA	HYPERTENSION	ENLARGEMENT OF HEART	ENDOCARDITIS, CHRONIC	AORTITIS, WITH DILATATION	PERICARDITIS, WITH EFFUSION	TACHYCARDIA	CARDIAC VALVULAR DISEASE, AORTIC STENOSIS	ADHERENT PERICARDIUM	ANEURYSM OF AORTA	MYOCARDITIS, ACUTE	HYDROPERICARDIUM	ANEURYSM OF AORTA, ASCENDING	ANEURYSM OF AORTIC ARCH	THROMBOPHLEBITIS, SAPHENOUS, *RIGHT INTERNAL BRANCH*	ARTERIOSCLEROSIS, CEREBRAL ARTERIES	HEART-BLOCK	ONLY ONE CARDIOVASCULAR LESION	TOTAL
Cardiac valvular disease, mitral insufficiency		2	16	1		2		1	1		1		1		1						1		1			167	195
Myocarditis, chronic, fibrous	12	2	1		3	3	4	6	6	1	2	1	1		1							1			1	74	119
Hypertrophy of heart	18			16	8	6			1	5		3		1				1	1							49	109
Cardiac valvular disease, aortic insufficiency	45	2	4			1	6						1	1		2		1						1		19	83
Enlargement of heart	3	12		5	2	1	1					2								1						7	34
Cardiac valvular disease, mitral stenosis	1	2		1	3			5																		21	33
Arteriosclerosis, general		4								2																14	20
Neurocirculatory asthenia																										17	17
Endocarditis, chronic	5		2		4						1															2	14
Aortitis, without dilatation					2	3			1																	8	14
Arrhythmia															1		1									10	12
Aortitis, with dilatation		1				1																				7	9
Adherent pericardium																										7	7
Hypertension		1				1																				5	7
Tachycardia																										7	7
Myocarditis, acute						1							1													4	6
Endocarditis, acute					1																					4	5
Arteriosclerosis, cerebral arteries							1																			4	5
Pericarditis, unclassified																	1									3	4
Auricular fibrillation			2						1																	1	4
Cardiac valvular disease, aortic stenosis			1	1																						1	3
Aneurysm of aortic arch						1				1																1	3

TABLE II—CONT'D

CARDIOVASCULAR DISEASE	CARDIAC VALVULAR DISEASE MITRAL INSUFFICIENCY	HYPERTROPHY OF HEART	CARDIAC VALVULAR DISEASE, MITRAL STENOSIS	MYOCARDITIS, CHRONIC	CARDIAC VALVULAR DISEASE, AORTIC INSUFFICIENCY	ARTERIOSCLEROSIS, GENERAL	AORTITIS, WITHOUT DILATATION	AURICULAR FIBRILLATION	ARRHYTHMIA	HYPERTENSION	ENLARGEMENT OF HEART	ENDOCARDITIS, CHRONIC	AORTITIS, WITH DILATATION	PERICARDITIS, WITH EFFUSION	TACHYCARDIA	CARDIAC VALVULAR DISEASE, AORTIC STENOSIS	ADHERENT PERICARDIUM	ANEURYSM OF AORTA	MYOCARDITIS, ACUTE	HYDROPERICARDIUM	ANEURYSM OF AORTA, ASCENDING	ANEURYSM OF AORTIC ARCH	THROMBOPHLEBITIS, SAPHENOUS, RIGHT INTERNAL BRANCH	ARTERIOSCLEROSIS, CEREBRAL ARTERIES	HEART-BLOCK	ONLY ONE CARDIOVASCULAR LESION	TOTAL
Atrophy of heart																										2	2
Fatty degeneration of heart											2																2
Congenital abnormality of the heart																										2	2
Thrombosis of left lenticulostriate artery																										2	2
Endocarditis, unclassified																										1	1
Cardiac valvular disease, pulmonic stenosis																										1	1
Pericarditis, fibrinous														1													1
Pericarditis with effusion																										1	1
Tumor of pericardium							1																				1
Aneurysm of aorta							1																				1
Aneurysm of aorta, ascending																										1	1
Cardiac murmur, functional																										1	1
Thromboangiitis obliterans																										1	1
Dextrocardia																										1	1
Endarteritis obliterans																										1	1
Hypotension																										1	1
Aneurysm of left occipital artery																										1	1
Aneurysm of pulmonary artery																										1	1
Thrombosis of striate arteries, ext. and int.																										1	1
Thrombosis of right lenticulostriate artery																										1	1
Thrombosis of femoral, saphenous and popliteal veins																										1	1
Thrombosis of veins of pelvis and legs																										1	1
TOTAL	84	26	26	24	23	20	14	12	10	9	6	6	4	3	3	2	2	2	1	1	1	1	1	1	1	453	736

TABLE III

SHOWING 301 CASES OF MITRAL INSUFFICIENCY, TOGETHER WITH ASSOCIATED CARDIOVASCULAR LESIONS

CARDIOVASCULAR DISEASE	CARDIOVASCULAR DISEASE													
	CARDIAC VALVULAR DISEASE, AORTIC INSUFFICIENCY	MYOCARDITIS, CHR. FIBROUS	HYPERTROPHY OF HEART	ARTERIOSCLEROSIS, GENERAL	ENDOCARDITIS, CHRONIC	AORTITIS, WITHOUT DILATATION	CARDIAC VALVULAR DISEASE, MITRAL STENOSIS	AORTITIS, WITH DILATATION	HYPERTENSION	AURICULAR FIBRILLATION	HEART-BLOCK	ONLY ONE COEXISTING CARDIOVASCULAR DISEASE	MITRAL INSUFFICIENCY WITHOUT COEXISTING C. V. DISEASE	TOTAL
Hypertrophy of heart	12	5		2	1							13		33
Cardiac valvular disease, aortic insufficiency							1					28		29
Cardiac valvular disease, mitral stenosis	4	2	2			1		1		1		12		23
Myocarditis, chr. fibrous	1		1	1	1							9		13
Enlargement of heart	1	1	2									4		8
Endocarditis, chronic	2											5		7
Arteriosclerosis, general		1	3						1			1		6
Aortitis, without dilatation	2	1												3
Aortitis, with dilatation	2											1		3
Aneurysm of aorta	1													1
Aneurysm of aorta, ascending												1		1
Endocarditis, chronic	1													1
Thrombophlebitis, right internal saphenous												1		1
Cardiac valvular disease, pulmonic stenosis	1													1
Hypertension	1													1
Auricular fibrillation												1		1
Tachycardia												1		1
Arrhythmia														1
Mitral insufficiency without coexisting c. v.											2			2
disease													167	167
Total	28	10	8	3	2	1	1	1	1	1	2	77	167	303

Associated Cardiovascular Lesions With Hypertrophy of Heart.—Table IV lists 148 cases of cardiac hypertrophy in such a manner as to show the various coexisting lesions. It is noted that 49 of these are cases of hypertrophy of heart without any other heart lesions; 39 had but one coexisting heart lesion, of this number 13 were cases of mitral insufficiency. Of the remaining 60 cases of hypertrophy of the heart having two coexisting heart lesions, the largest group is a combination of mitral insufficiency, aortic insufficiency, and hypertrophy of the heart.

Associated Cardiovascular Lesions With Chronic Myocarditis.—Table V lists 153 cases of chronic myocarditis arranged in such a manner as to show the various combinations of lesions. It is noted that 74 were cases of chronic myocarditis without any coexisting heart lesions; 43 cases of chronic myocarditis had but one coexisting lesion, of which number, that of chronic myocarditis with mitral insufficiency, was the largest group; 36 cases of chronic myocarditis had two coexisting heart lesions, the largest group of which was a combination of hypertrophy of the heart, enlargement of the heart, and chronic myocarditis.

Associated Cardiovascular Lesions With Aortic Insufficiency.—Table VI lists 111 cases of aortic insufficiency in such a manner as to show the various combinations of cardiovascular lesions. It is noted that of the total number, 19 are aortic insufficiency without any coexisting heart lesions; there are 52 cases of aortic insufficiency with but one coexisting lesion, the largest group of which is that of mitral insufficiency. Of those cases of aortic insufficiency with two coexisting heart lesions, 40 in number, the largest group is a combination of hypertrophy of the heart, mitral insufficiency, and aortic insufficiency.

ETIOLOGICAL TYPES OF HEART DISEASE

Wyckoff and Lingg[3] in their study of the distribution of 1051 cases of heart disease found that 42.7 per cent were of the rheumatic type; 22.2 per cent of the arteriosclerotic type; 8.6 per cent were of the syphilitic type; 8.6 per cent belonged to other etiological types, and 17.8 per cent of the heart lesions were of unknown etiology.

Haven Emerson,[4] after a review of the histories of 927 adults with heart disease, found the distribution of the causative factors as follows:

Acute rheumatic fever	331
Acute tonsillitis	207
Carious teeth	163
Syphilis	122
Scarlet fever	78
Measles	54
Diphtheria	47
Pertussis	14
Chorea	7
Total	1023

The above figures would indicate that more than one etiological factor was the cause of the heart lesions in a number of the patients.

TABLE IV

SHOWING 148 CASES OF HYPERTROPHY OF HEART, TOGETHER WITH ASSOCIATED CARDIOVASCULAR LESIONS

CARDIOVASCULAR DISEASE	CARDIAC VALVULAR DISEASE, MITRAL INSUFFICIENCY	ARTERIOSCLEROSIS, GENERAL	ENLARGEMENT OF HEART	AORTITIS, WITH DILATATION	HYPERTENSION	MYOCARDITIS, CHR. FIBROUS	CARDIAC VALVULAR DISEASE, AORTIC INSUFFICIENCY	CARDIAC VALVULAR DISEASE, MITRAL STENOSIS	ARRHYTHMIA	FATTY INFILTRATION OF HEART	EMBOLISM OF MIDDLE CEREBRAL ARTERY	ONLY ONE COEXISTING CARDIOVASCULAR DISEASE	HYPERTROPHY OF HEART WITHOUT COEXISTING C. V. DISEASE	TOTAL
Myocarditis, chr. fibrous	5	1	7	1			2		1	1	1	6		25
Cardiac valvular disease, mitral insufficiency		3	2			1		2				13		21
Cardiac valvular disease, aortic insufficiency	12			1								3		16
Hypertension		6				1						5		12
Arteriosclerosis, general	2				3							3		8
Endocarditis, chronic	1		1									2		4
Enlargement of heart												2		2
Aortitis, without dilatation		2												2
Cardiac valvular disease, mitral stenosis												2		2
Myocarditis, acute												1		1
Arteriosclerosis, local				1										1
Aneurysm of aorta												1		1
Aneurysm of aortic arch		1												1
Pericarditis, with effusion		1												1
Auricular fibrillation									1					1
Arrhythmia												1		1
Hypertrophy of heart without coexisting c. v. disease													49	49
Total	20	14	10	3	3	2	2	2	2	1	1	39	49	148

TABLE V

SHOWING 153 CASES OF CHRONIC MYOCARDITIS TOGETHER WITH ASSOCIATED CARDIOVASCULAR LESIONS

CARDIOVASCULAR DISEASE	CARDIOVASCULAR DISEASE												
	HYPERTROPHY OF HEART	CARDIAC VALVULAR DISEASE, MITRAL INSUFFICIENCY	ENLARGEMENT OF HEART	AORTITIS, WITHOUT DILATATION	CARDIAC VALVULAR DISEASE, MITRAL STENOSIS	HYPERTENSION	ARRHYTHMIA	ARTERIOSCLEROSIS, GENERAL	ARTERIOSCLEROSIS, LOCAL	AURICULAR FIBRILLATION	ONLY ONE COEXISTING CARDIOVASCULAR DISEASE	CHRONIC MYOCARDITIS WITHOUT COEXISTING C. V. DISEASE	TOTAL
Cardiac valvular disease, mitral insufficiency	5		1	1	2			1			9		19
Enlargement of heart	7										5		12
Hypertrophy of heart		1				1					6		8
Arrhythmia	1					1					5		7
Auricular fibrillation											6		6
Arteriosclerosis, general	1	1	1						1		1		5
Cardiac valvular disease, aortic insufficiency	2	1		1							1		5
Aortitis, without dilatation							1				3		4
Cardiac valvular disease, mitral stenosis										1	2		3
Aortitis, with dilatation	1										1		2
Fatty infiltration of heart	1												1
Endocarditis, chronic		1											1
Aneurysm of aortic arch											1		1
Embolism of middle cerebral artery	1												1
Cardiac valvular disease, aortic stenosis											1		1
Hypertension											1		1
Heart-block							1						1
Tachycardia											1		1
Chronic myocarditis without coexisting c.v. disease												74	74
Total	19	4	2	2	2	2	2	1	1	1	43	74	153

TABLE VI

SHOWING 111 CASES OF AORTIC INSUFFICIENCY TOGETHER WITH ASSOCIATED CARDIOVASCULAR LESIONS

CARDIOVASCULAR DISEASE	CARDIOVASCULAR DISEASE: HYPERTROPHY OF HEART	ENDOCARDITIS, CHRONIC	MYOCARDITIS, CHRONIC FIBROUS	CARDIAC VALVULAR DISEASE, MITRAL STENOSIS	ENLARGEMENT OF HEART	AORTITIS, WITHOUT DILATATION	AORTITIS, WITH DILATATION	ANEURYSM OF AORTA	ANEURYSM OF ULNAR ARTERY	ENDOCARDITIS, ACUTE	CARDIAC VALVULAR DISEASE, MITRAL INSUFFICIENCY	CARDIAC VALVULAR DISEASE, PULMONIC STENOSIS	HYPERTENSION	ONLY ONE COEXISTING CARDIOVASCULAR DISEASE	AORTIC INSUFFICIENCY WITHOUT COEXISTING C. V. DISEASE	TOTAL
Cardiac valvular disease, mitral insufficiency	12	2	1	4	1	2	2	1		1		1	1	28		56
Aortitis, without dilatation		1	1											8		10
Cardiac valvular disease, mitral stenosis									1		1			5		7
Hypertrophy of heart			2											3		5
Enlargement of heart		2												1		3
Cardiac valvular disease, aortic stenosis					1									2		3
Arteriosclerosis, general		1												1		2
Aortitis, with dilatation	1													1		2
Myocarditis, chronic														1		1
Aneurysm of aorta		1														1
Arteriosclerosis, local														1		1
Pericarditis, with effusion														1		1
Aortic insufficiency without coexisting c. v. disease															19	
Total	13	7	4	4	2	2	2	1	1	1	1	1	1	52	19	111

Acute rheumatic fever, acute tonsillitis, and carious teeth exceeded other causes of heart disease in the 927 cases referred to by Dr. Emerson.

In a statistical study of 3000 patients with heart disease in New England, some of whom were patients at the Massachusetts General Hospital and others were private patients seen in consultation, Paul D. White[5] found that 54.5 per cent were of the rheumatic type. This observer maintains that the large percentage of rheumatic heart disease is due to climate, social and economic abnormalities, family susceptibility, and a probable mild contagious character of rheumatic fever. Coronary disease was the cause of heart lesions in 20.5 per cent of the cases; hypertension in 31 per cent; syphilis in 4 per cent; hyperthyroidism in 3 per cent; subacute bacterial endocarditis in 2 per cent; angina pectoris (hospital patients) in 9.5 per cent; angina pectoris (private patients) in 21 per cent; coronary thrombosis in from 3 to 6 per cent, and in 2.5 per cent of the cases the etiological factor was unknown.

In an analysis of 360 cases of valvular heart disease discharged from the U. S. Navy, Bloedorn and Roberts[6] found the principal etiological factors as follows: Rheumatic fever was the etiological factor in 101 cases; tonsillitis in 59; syphilis in 3; pneumonia in 4, and influenza in 4.

Wycoff and Lingg,[3] in a series of 499 cases of heart disease, found that 59.7 per cent were due to acute rheumatic fever and 12.7 per cent were due to tonsillitis. It is noted that in the group of cases studied by these observers no case of heart disease was attributed to diseases of the teeth and gums.

Table VII is a classification of heart disease found among 736 Bureau beneficiaries into 11 types of etiological factors, similar to that used by the American Heart Association. Attention is invited to the fact that in a number of cases two or more etiological factors

TABLE VII

ETIOLOGICAL TYPES OF HEART DISEASE IN 736 BUREAU PATIENTS WITH 1761 ETIOLOGICAL FACTORS, SHOWING PER CENT OF TOTAL NUMBER WITHIN EACH TYPE

ETIOLOGICAL TYPE	NUMBER	PER CENT
Rheumatic	590	33.50
Other infectious diseases	529	30.04
Syphilitic	197	11.19
General systemic disease	76	4.32
Arteriosclerotic	71	4.03
Toxic	35	1.99
Traumatic	34	1.93
Thyroid	23	1.31
Neurogenic	15	0.85
Others	45	2.55
Unknown	146	8.29
Total	1761	100.00

were present, making a total of 1761 factors in a series of 1123 lesions. The average number of etiological factors per lesion was 1.56, and the average number of etiological factors per patient was 2.39.

A review of Table VII indicates that the principal etiological factors of heart disease as found in a series of ex-service men of an average age of thirty-six are: rheumatism, other infectious diseases, and syphilis. Attention is invited to the fact that arteriosclerosis was an etiological factor to the extent of 4.03 per cent only.

Rheumatic Heart Disease.—Table VIII lists rheumatic heart disease according to the types of infection. It is noted that tonsillitis, acute rheumatic fever, and tooth and gum infections constitute the principal etiological factors in 83.22 per cent of a series of 590 cases of rheumatic heart disease.

The incidence of the other etiological rheumatic factors was of minor importance. Reference to Table VIII shows that they comprise only 99, or 16.78 per cent, of the total number of rheumatic factors in the series of cases studied.

TABLE VIII

RHEUMATIC HEART DISEASE BY TYPE OF INFECTION SHOWING PER CENT OF EACH TYPE

TYPE OF INFECTION	NUMBER	PER CENT
Tonsillitis	238	40.34
Acute rheumatic fever	131	22.20
Tooth and gum infections	122	20.68
Joint pains	35	5.93
Muscle pains	19	3.22
Pharyngitis	11	1.86
Arthritis	11	1.86
Rheumatic nodules	8	1.36
Chorea	8	1.36
Osteoarthritis	4	0.68
Torticollis	1	0.17
Diseased adenoids	1	0.17
Myositis	1	0.17
Total	590	100.00

Heart Disease, the Sequel of Infectious Diseases.—While the part played by the infectious diseases as etiological factors of heart disease is based upon the histories of the cases as obtained from the patients, in a large number the causative infectious disease was incurred in the military service, and was followed by the heart lesion reported on the questionnaire. Most of the data are on record and therefore dependable.

A study of the data recorded in this paper indicates that the other infectious diseases constitute a group of etiological factors of heart disease second only to the rheumatic infections.

Whether heart lesions due to infectious diseases are latent for a long period and become clinically apparent only some time after the

occurrence of the infectious disease is yet to be ascertained. According to data in Table IX, one would infer that such is a possibility.

Table IX lists the infectious diseases which were considered etiological factors of heart disease in this study. It is noted that the incidence of influenza as an etiological factor of infectious heart disease was very great—in fact it was given as the cause of heart disease in 167, or 31.57 per cent, of a series of 529 cases.

Some of the other principal causative infectious diseases were: pneumonia, tuberculosis, measles, typhoid fever, gonorrhea and otitis media.

TABLE IX

HEART DISEASE, THE SEQUEL OF INFECTIOUS DISEASES, BY TYPE OF DISEASE

INFECTIOUS DISEASE	NUMBER	PER CENT
Influenza	167	31.57
Pneumonia	85	16.07
Tuberculosis	75	14.18
Measles	42	7.94
Typhoid fever	32	6.05
Gonorrhea	31	5.86
Otitis media	28	5.29
Scarlet fever	25	4.73
Diphtheria	18	3.40
Dysentery	16	3.02
Mumps	5	0.94
Amebiasis	2	0.38
Cerebrospinal meningitis	1	0.19
Malaria	1	0.19
Dengue	1	0.19
Total	529	100.00

INTERVAL BETWEEN OCCURRENCE OF ETIOLOGICAL FACTOR AND APPEARANCE OF CARDIOVASCULAR DISEASE

Haven Emerson[4] in an analysis of 100 cases of rheumatic heart disease for the purpose of ascertaining the length of time elapsing between the date of probable infection and knowledge of cardiac disease found that the average period was 5.36 years. The periods varied widely from patients where knowledge was immediate at the time of the acute sickness to those who had evidently had their disease thirty years before knowledge of it was obtained.

Emerson also found that in the case of 23 patients with syphilitic heart disease the average time before knowledge of the cardiac disease was obtained was 17.65 years, the range being from one to thirty-four years.

Cohn, quoting Mackie,[7] says that among 25 cases of mitral stenosis the lesion was developed within twenty-four months in 22 cases, but that it required five and a half, six and a half and five and two-thirds years in the 3 additional cases. It may then take from one to six years for the cardiac lesions to develop; meanwhile manifestations of rheumatic disease may be quite absent.

Table X illustrates the interval between the operation of the etiological factors and the recognition of the cardiovascular lesions in a series of 736 patients. In considering the entire group of 1761 etiological factors, it is noted that in 886 instances it was impossible to determine the interval between the occurrence of the etiological factor and the appearance of the cardiovascular disease. Of the remainder, 875 in number, the physicians were able to record the time interval. Of this number, in 108 instances the heart lesion developed immediately; in 26 instances within one month; in 59 instances between one and three months; in 34 between three and six months; in 21 between six and twelve months; in 325 between one and five years; in 229 between five and ten years; and in 73 instances between ten and twenty-five years.

It is believed that these data when critically analyzed are subject to question. What the mechanism is in the production of a heart lesion a number of years after the occurrence of the infection is not known. Perhaps the heart valve is affected at the time of the appearance of the disease without giving any clinical evidence. These figures, therefore, should be interpreted as indicating the time between the occurrence of the etiological disease and the clinical recognition of the heart lesion.

Further analysis of the data in Table X would lead one to assume that the interval of time elapsing between the occurrence of the etiological disease and the appearance of the cardiac lesion is dependent upon several factors: first, the type of causative disease; second, extent of degenerative changes and location of heart lesion; and finally, the rapid or slow development of cardiac lesions is dependent upon the amount of functional activity to which the heart is subjected. If the heart lesion is slight, it is thought the damage might not be sufficient to bring about abnormal cardiac function; if the latter becomes apparent, it would be some time after the occurrence of the causative disease. On the other hand, if the heart which had undergone certain abnormal changes, even though slight, were subjected to excessive physical strain, cardiac derangement sufficient to be recognized clinically might appear early.

DURATION OF CARDIOVASCULAR DISEASE

Any discussion of the duration of heart disease in ex-service men must be cautious, because of the fact that a great many of the patients attribute the heart disease to increased physical effort or to diseases incurred while in the military service. This is to be expected. While in the majority of instances the data are reliable, in some, the findings may be questionable. However, in spite of this, the figures in Table XI give an approximate idea of the duration of cardiovascular disease

TABLE X

INTERVAL BETWEEN OCCURRENCE OF ETIOLOGICAL FACTOR AND APPEARANCE OF CARDIOVASCULAR DISEASE IN 736 PATIENTS WITH 1761 ETIOLOGICAL FACTORS

ETIOLOGICAL FACTOR	IMMEDIATELY	LESS THAN 1 MO.	1 TO 3 MO.	3 TO 6 MO.	6 TO 12 MO.	1 TO 2 YR.	2 TO 3 YR.	3 TO 4 YR.	4 TO 5 YR.	5 TO 6 YR.	6 TO 7 YR.	7 TO 8 YR.	8 TO 10 YR.	10 TO 25 YR.	UNKNOWN INTERVAL	TOTAL	PER CENT
Rheumatic	49	15	23	15	14	53	21	19	18	10	18	5	36	31	263	590	33.50
Infectious diseases	29	10	27	16	7	64	20	20	17	12	14	7	26	31	229	529	30.04
Syphilitic	3		4	2		10	5	4		4	9	7	42	2	105	197	11.19
General systemic disease	10			1		12	10	2	3		4		2		32	76	4.32
Arteriosclerotic	3					6	6		3		5		3	1	44	71	4.03
Toxic	3	1				1		1		3	2	1	6		17	35	1.99
Traumatic	6		1			2	3	2	2		2		2	1	13	34	1.93
Thyroid			3			4	2					1	3		10	23	1.31
Neurogenic	3		1			3					1			1	6	15	0.85
Others	2					3	6	3		2			2	6	21	45	2.55
Unknown factor															146	146	8.29
Total	108	26	59	34	21	158	73	51	43	31	55	21	122	73	886	1761	100.00

in these 736 patients. It is noted that of the total number it was impossible to determine the duration of heart disease in 245 cases. In the remainder, namely, 491 cases, heart disease existed for periods varying from one to six months in 30 cases to from eight to nine years in 41 cases; in 3 cases the heart disease was congenital; the largest group, 85 in number, gave a history of having had heart disease from seven to eight years.

TABLE XI

TABLE SHOWING DURATION OF CARDIOVASCULAR DISEASE IN A GROUP OF 736 PATIENTS

	NUMBER OF CASES
Congenital	3
1 to 6 months	30
6 to 12 months	47
1 to 2 years	31
2 to 3 years	51
3 to 4 years	29
4 to 5 years	47
5 to 6 years	54
6 to 7 years	73
7 to 8 years	85
8 to 9 years	41
Time not known	245
Total	736

Table XII gives a list of the specific heart diseases in a series of 255 of the total number of 736 patients. These patients were hospitalized primarily for heart disease.

In the consideration of these 255 cases it is realized, of course, that the date of diagnosis of the heart disease was not necessarily the date of its inception. For instance, the duration of chronic myocarditis, combined aortic and mitral disease, and of mitral insufficiency, as indicated in Table XII, is very much shorter than is the customary clinical experience. It is thought that in a number of these cases the heart lesions were present some time before they were recognized clinically. The figures, however, serve their purpose in showing the clinical duration of certain cardiovascular lesions among ex-service men hospitalized by the United States Veterans Bureau.

A study was also made of the duration of various cardiovascular lesions in 252 Bureau beneficiaries who died from heart disease. The time from the date of diagnosis of the lesion to the date of death was as follows:

For acute dilatation of the heart—eight months; acute endocarditis—four months; chronic endocarditis—four years; cerebral hemorrhage—two years; acute myocarditis—two years; chronic myocarditis—four years; combined aortic and mitral disease—five years; and mitral insufficiency—three years.

TABLE XII

Duration of Cardiovascular Disease in 255 of 736 Patients Showing Specific Cardiovascular Diagnosis

Cardiovascular Disease	1 to 6 Mo.	6 Mo. to 1 Yr.	1 to 2 Yr.	2 to 3 Yr.	3 to 4 Yr.	4 to 5 Yr.	5 to 6 Yr.	6 to 7 Yr.	7 to 8 Yr.	8 to 9 Yr.	Unknown	Not Reported	Total
Myocarditis, chronic	3	6	5	6	1	5	6	7	9	4	6	1	59
Valvular heart disease, combined lesions, aortic and mitral		2	3	2	2	7	7	8	10	5	3		49
Valvular heart disease, mitral insufficiency	1	2		3	1	3	7	9	9	4	6		45
Valvular heart disease, aortic insufficiency	1	1	1	2	3	3	2	2	4	1	1		21
Valvular heart disease, mitral stenosis		3		3	2	1	2	7		1		1	20
Aortitis			1		3				1		2		7
Asthenia, neurocirculatory							1	2		1	2	1	7
Auricular fibrillation					1	1	1	1	2		1		7
Aneurysm, aorta		1		1		1			2		1		6
Hypertension					1		1		1	1	1	1	6
Arteriosclerosis, general									2		2		4
Cardiac arrhythmia, otherwise unclassified				1					1		1		3
Cardiac hypertrophy							1	2					3
Endocarditis, septic		1									1	1	3
Arteriosclerosis, cerebral				1						1			2
Cardiac hypertrophy and dilatation									1		1		2
Myocarditis, acute	1										1		2
Pericarditis, with effusion	1	1											2
Tachycardia							1		1				2
Dilatation, aortic arch				1									1
Endocarditis, chronic							1						1
Heart-block									1				1
Valvular heart disease, aortic stenosis											1		1
Valvular heart disease, otherwise unclassified									1				1
Total	7	17	10	20	14	21	30	38	45	18	30	5	255

These 252 beneficiaries were not part of the group of 736 cases previously referred to, but were a group arbitrarily selected for the purpose of ascertaining the period of time elapsing between the date of diagnosis of heart disease and date of death. Attention is invited to the fact that the duration of the various heart lesions is shorter than is the usual experience. The figures are, however, the actual clinical experience in the case of these 252 ex-service patients.

FUNCTIONAL CAPACITY IN CARDIOVASCULAR DISEASE

The statistics appearing in Table XIII consist of the data received from the various Bureau hospitals. The classification of the functional capacity of ex-service patients with cardiovascular disease is in accordance with the standards recommended by the American Heart Association.

In the consideration of the total number of patients it is noted that 209, or 28.40 per cent, were able to carry on their habitual physical activity; 218, or 29.62 per cent, were able to carry on a slightly diminished activity, and were therefore placed in Class 2-A; 142, or 19.29 per cent, were able to carry on a greatly diminished activity, and were therefore grouped in Class 2-B; whereas 82, or 11.14 per cent, were unable to carry on any physical activity, were confined to bed, and were grouped in Class 3; in 85, or 11.55 per cent, of the patients the functional capacity was not stated.

It is seen, therefore, that 442, or 60.05 per cent, of the whole group of 736 patients had various heart lesions which resulted in a reduced functional activity. These patients were classified as belonging to Groups 2-A, 2-B, and 3—such classification denotes that their earning capacity is impaired.

The Bureau has, therefore, a twofold problem to solve: first, how best to rehabilitate these patients physically; second, how to restore them to a state of maximum economic efficiency. The physical rehabilitation can be accomplished by the excellent hospital facilities of the Bureau available throughout the country, where the patients with decompensation may be treated and restored to efficient cardiac function. This can be supplemented by the utilization of the dispensary facilities in the regional offices where these patients may be further treated and observed until they attain maximum cardiac improvement.

During hospitalization these cardiac patients may be instructed in various light occupational crafts, and an attempt could be made to ascertain the maximum physical effort which may be expended by the patient as well as his work tolerance. The occupations prescribed by the physician as therapy in the hospital can be so arranged as to assist in determining the vocational potentiality of the patient.

Upon restoration of the patient to normal cardiac function, the physician as well as the occupational therapy aide and also the social worker in the hospital should study the individual case for the purpose of ascertaining suitable vocational placement. It is important that the Bureau supervise closely the employment of these cardiac cases after their discharge from hospitalization. These patients should be urged to return periodically either to the out-patient department of the hospital or to the dispensary of the regional office for cardiac examinations, so that the effect of work upon the circulatory system may be determined. If it is found that the physical effort expended in this direction is causing decompensation, the physician as well as the social worker should urge the patient to change the character, or the amount, of work.

It is believed that by such a procedure not only would the lives of many of these patients be prolonged and saved, but, in many instances, hospitalization would be resorted to less frequently and the amount of financial compensation might be reduced because of a decrease of the occupational handicap and an increase in work tolerance.

The above views are predicated upon that section of the World War Veterans Act which states that "The Bureau will have the power and it will be its duty to provide for the placement of rehabilitated persons in suitable and gainful occupations." Based on the above, the Director of the U. S. Veterans Bureau wisely promulgated a letter dated December 14, 1927, to regional managers. He stated therein that it was his desire that contacts be established with a view of assisting veterans in obtaining employment. He requested that a close cooperation be established with civilian agencies for the purpose of placing disabled ex-service men in suitable and gainful occupations.

The Director in issuing this letter evidently felt that the responsibility of the Bureau did not cease with the hospitalization and compensation of these disabled ex-service men, but that the facilities of the Bureau should be extended still further with a view of prolonging the lives of these patients and guiding them through occupational hazards. This, if properly done, will result not only in direct benefit of patients, but indirectly in an economic saving to the government.

EFFECT OF TONSILLECTOMY ON HEART DISEASE

In view of the fact that tonsillitis was considered an etiological factor in 238, or 40.3 per cent, of 590 cases of rheumatic heart disease, it was thought that a study should be made of the effect of tonsillectomy upon the course of the disease and upon the final outcome of the case.

TABLE XIII

SHOWING FUNCTIONAL CAPACITY OF 736 EX-SERVICE PATIENTS WITH CARDIOVASCULAR DISEASE, ACCORDING TO THE CLASSIFICATION OF THE AMERICAN HEART ASSOCIATION

	ABLE TO CARRY ON HABITUAL PHYSICAL ACTIVITY (1)	ABLE TO CARRY ON SLIGHTLY DIMINISHED PHYSICAL ACTIVITY (2A)	ABLE TO CARRY ON GREATLY DIMINISHED PHYSICAL ACTIVITY (2B)	UNABLE TO CARRY ON ANY PHYSICAL ACTIVITY (3)	NOT STATED	TOTAL	PER CENT
Mitral insufficiency	84	72	24	8	7	195	26.49
Myocarditis, chronic, fibrous	21	36	28	18	16	119	16.16
Hypertrophy of heart	26	37	24	13	9	109	14.81
Aortic insufficiency	19	25	18	11	10	83	11.27
Enlargement of heart	5	5	11	5	8	34	4.62
Mitral stenosis	6	7	5	6	9	33	4.48
Arteriosclerosis, general	7	5	5	2	1	20	2.71
Neurocirculatory asthenia	4	3	3		7	17	2.31
Endocarditis, chronic	4	3	4	2	1	14	1.90
Aortitis, without dilatation	6	4		2	2	14	1.90
Arrhythmia	6	3	3			12	1.63
Aortitis, with dilatation	3	3	1	2		9	1.22
Adherent pericardium	3	2	2			7	0.95
Hypertension	4	2	1			7	0.95
Tachycardia	3	2	1		1	7	0.95
Myocarditis, acute		1	2	2	1	6	0.81
Arteriosclerosis, cerebral arteries	2	1	1	1		5	0.68
Endocarditis, acute				1	4	5	0.68
Auricular fibrillation	1	2		1		4	0.54
Pericarditis, unclassified	1	1	2			4	0.54
Aortic stenosis		2		1		3	0.40

TABLE XIII—CONT'D

	ABLE TO CARRY ON HABITUAL PHYSICAL ACTIVITY (1)	ABLE TO CARRY ON *SLIGHTLY* DIMINISHED PHYSICAL ACTIVITY (2A)	ABLE TO CARRY ON GREATLY DIMINISHED PHYSICAL ACTIVITY (2B)	UNABLE TO CARRY ON ANY PHYSICAL ACTIVITY (3)	NOT STATED	TOTAL	PER CENT
Aneurysm of aortic arch				3		3	0.40
Atrophy of heart	2					2	0.27
Congenital abnormality of heart		1			1	2	0.27
Fatty degeneration of heart					2	2	0.27
Thrombosis of left lenticulostriate artery			1	1		2	0.27
Thrombosis of right lenticulostriate artery			1			1	0.14
Cardiac murmur, not organic					1	1	0.14
Dextrocardia			1			1	0.14
Pericarditis, fibrinous				1		1	0.14
Pericarditis, with effusion				1		1	0.14
Pulmonic stenosis	1					1	0.14
Tumor of *pericardium*					1	1	0.14
Aneurysm of *aorta*					1	1	0.14
Aneurysm of aorta, ascending			1			1	0.14
Aneurysm of left occipital artery	1					1	0.14
Aneurysm of pulmonary *artery*					1	1	0.14
Thrombosis *of striate* arteries, external and internal				1		1	0.14
Thrombosis of femoral, saphenous, and popliteal veins					1	1	0.14
Thrombosis of veins of pelvis and leg					1	1	0.14
Endarteritis obliterans			1			1	0.14
Endocarditis, unclassified			1			1	0.14
Hypotension		1				1	0.14
Thromboangiitis obliterans			1			1	0.14
Total	209	218	142	82	85	736	100.00

A number of observers have made similar studies of this problem and the conclusions reached have been at variance with each other.

Cohn[2] refers to 391 patients with rheumatic manifestations on whom tonsillectomy was done, with subsequent observations. The rheumatic manifestations for which the operation was performed recurred in 49.6 per cent of the cases.

In 175 patients with rheumatic manifestations on whom tonsillectomy was not done, 111, or 64 per cent, suffered from a recurrence of the disease. Cohn finds from a study of the cases reported by certain observers that, on the whole, it cannot be said that the effect upon rheumatic fever of the removal of the tonsils is satisfactory, inasmuch as recurrence of rheumatic manifestations takes place in 50 per cent of the cases.

St. Lawrence[8] observed 58 cases of organic cardiac disease before and after tonsillectomy and found that, in general, there seemed to be a fairly prompt increase both in desire and in capacity for exertion; and the exercise tolerance seemed to be favorably influenced more often, more promptly, and to a greater degree by tonsillectomy than by any other measure utilized in the care of cardiac children. In a series of 5 cases it was observed that an incomplete removal of the tonsils had little or no effect on the recurrence, while complete tonsillectomy was followed by a cessation of the symptoms of heart disease.

Crowe, Watkins, and Rothholz, quoted by Cohn,[9] noted recurrences of rheumatic fever in 4 out of 25 cases under observation; these occurred from three weeks to three years after tonsillectomy. In all of the 25 cases, except 4, there were cardiac lesions present; mitral lesions were present in 21; some of the patients had 2 or more coexisting cardiac lesions.

Of 24 cases of chorea with concomitant heart lesions, in 12 cases the same authors report that chorea recurred or failed to disappear in 11 instances ranging from eight months to three and one-sixth years after tonsillectomy.

A study of the Bureau statistics revealed the fact that tonsillectomy was done on 220 out of the total number of 736 patients under observation. One hundred and thirty-seven of this number had heart lesions prior to tonsillectomy; in 44 instances the heart lesions were first noted after the removal of the tonsils. In 15 the time of the first appearance of the heart lesion was unknown; and in 24 instances no report was made.

A review of the available data further shows that in 145 cases it was the opinion of the Bureau physicians that the cardiovascular disease was due primarily to tonsillitis, and that tonsillectomy had the following effect:

Improved	18
Retrogressed	7
No change	28
Undetermined	7
Not stated	85

The above figures would indicate that the Bureau physicians found it difficult, in a number of instances, to attribute to the tonsillectomy any effect upon the cardiovascular disease. However, in 18, or 12.4 per cent, of the cases it was thought that improvement followed the operation. This estimate it is believed is conservative. It would appear, therefore, that if infected tonsils are an etiological factor of heart disease, their removal is followed by an improvement in a small percentage of cases.

(To be continued in April.)

ELECTROCARDIOGRAPHIC STUDIES ON THE ACTIONS OF DRUGS

I. The Vagus in Ether Anesthesia*

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THE present study was undertaken to determine the influence of ether in the various stages of anesthesia upon the response of the vagus (cardio-inhibitory nerve) to stimulation by morphine.

Fifteen experiments were carried out on dogs, only those animals that were found to remain quiet without anesthesia or restraint being employed. Ether was given by inhalation (open cone), always with sufficient air to avoid asphyxial changes. Electrocardiograms (Lead II only was used) were taken at frequent intervals, and changes in the sinus rate and conduction time (P-R intervals) were noted. Since there are frequently considerable differences in the length of the P-R interval from beat to beat, ten such intervals in a given strip were determined, and the average was taken as the interval for that observation. Where several experiments were performed on the same dog a number of days intervened between them. Observations made in five of the experiments will be given in detail, as they suffice to illustrate the general results.

In the first experiment a dog (A) received 1 mg. of morphine sulphate per kg. intravenously, and within twenty-seven minutes the sinus rate had decreased from 180 to 80 a minute and the P-R interval had increased from 0.093 to 0.108 second, and there were some dropped ventricular groups. During the early stage of ether anesthesia nearly all the morphine effects disappeared and remained in abeyance during the period of deep ether narcosis. The T-wave showed interesting changes. In the control period it was negative and 1 mm. deep. During the morphine action it became 3 mm. deep. During the early stage of ether inhalation the morphine effect upon the T-wave persisted. In the stage of deep ether narcosis (corneal reflexes abolished, pupils dilated and not reacting to light, complete muscular relaxation, respiration good), the morphine effect upon the T-wave disappeared and the latter assumed the form present in the control period. Ether,

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therefore, in this experiment completely abolished the effects of morphine stimulation of the vagus. (See Figs. 1 and 2.)

In the second experiment the order was reversed, the same animal being anesthetized to deep ether narcosis before the morphine was administered. Ether increased the heart rate markedly and shortened the P-R interval. These effects established during the excitement stage of ether action persisted during the period of deep narcosis. Morphine sulphate (1 mg. per kg. intravenously) abolished the ether effect upon the heart rate and conduction, both factors returning to the level of

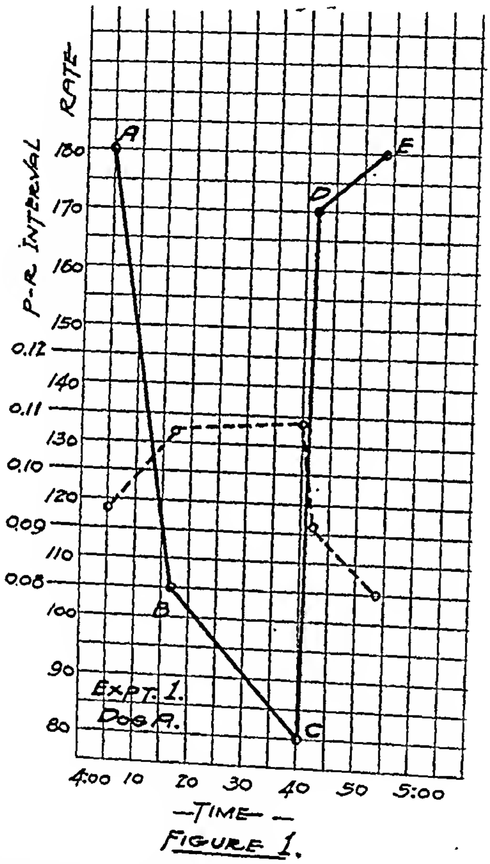

Fig. 1.—*A*, Control; *B*, five minutes after 1 mg. morphine sulphate per kg. intravenously, dropped ventricular groups; *C*, dropped ventricular groups; *D*, two minutes after starting inhalation of ether, struggling; *E*, deep ether anesthesia.

the control tracing, and during one-half hour of deep ether narcosis morphine produced no further effect. This is in striking contrast to the intensity of the effect of the same dose of morphine in the same dog in the first experiment, without ether. A second dose of morphine (2 mg. per kg. intravenously) caused a further decrease in the heart rate and increase in P-R interval, but the changes were not nearly so marked as those produced by one-half the dose of morphine in the same dog without ether. With the recovery from the ether the morphine effects became more pronounced. This experiment, therefore, shows that in the presence of ether narcosis morphine may produce

some vagal effects but much less intense than in the unanesthetized animal. (See Fig. 3.)

The third experiment shows essentially the same phenomena as the first. A second dose of morphine was given which produced primary acceleration of the heart rate and shortening of the P-R interval.

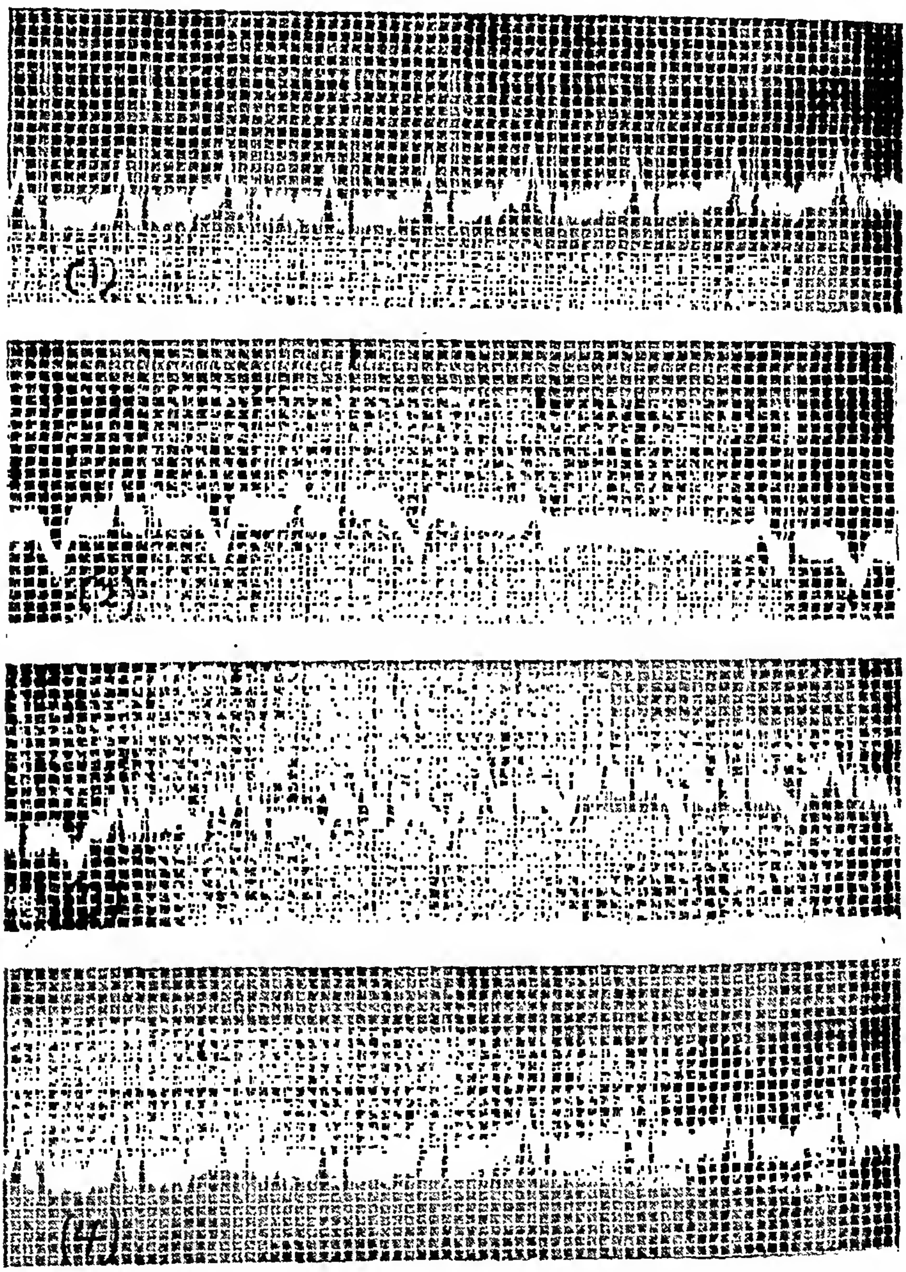

Fig. 2.—*1*, Control; *2*, after 1 mg. morphine sulphate per kg. intravenously; *3*, light ether anesthesia; *4*, deep ether anesthesia.

This occurred in the absence of any signs of nausea or vomiting. It was followed by complete A-V block. Three minutes after the inhalation of ether was started the block was abolished, and the heart rate and P-R interval returned to the level present in the control period.

After a lapse of about three and one-half hours during which the animal recovered from the anesthesia, morphine effects upon the vagus were again in evidence. These effects were completely abolished after paralysis of the vagal endings by atropine. (See Fig. 4.)

In the fourth experiment a dog (B) received a dose of 20 mg. morphine sulphate per kg. subcutaneously. One hour later, during morphine narcosis, the tracing showed a very slow sinus rate (55 per minute) and long P-R interval (0.16 second). Three minutes after beginning the inhalation of ether (light anesthesia), the sinus rate had doubled, but the P-R interval, which ordinarily shortens with increase

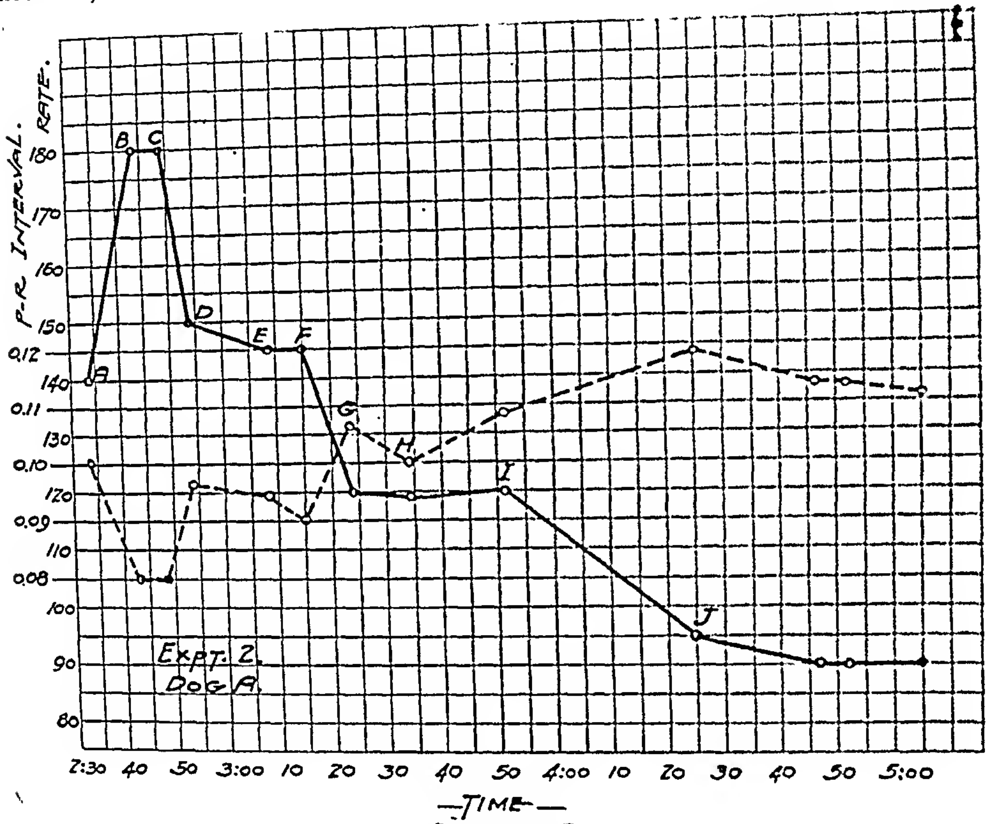

FIGURE 3.

Fig. 3.—*A*, Control; *B*, nine minutes after starting inhalation of ether, corneal reflexes abolished; *C*, deep ether anesthesia; *D*, four minutes after 1 mg. morphine sulphate per kg. intravenously during deep ether anesthesia; *E*, and *F*, deep ether anesthesia; *G*, five minutes after 2 mg. morphine sulphate per kg. intravenously during deep ether anesthesia; *H*, deep ether anesthesia; *I*, seven minutes after ether discontinued; *J*, recovered from ether anesthesia.

in the rate, in this instance was lengthened to 0.24 second. During deep ether narcosis the sinus rate remained rapid and the P-R interval shortened to that present before the ether. In this experiment, therefore, the effect of a very large dose of morphine upon the sinus rate was abolished by the ether, while that upon conduction showed initial accentuation but at no time any diminution. Paralysis of the vagal endings by atropine produced further acceleration of the sinus rate (140 to 170) while the P-R interval diminished from 0.182 to 0.102 second. (See Fig. 5.)

In the fifth experiment an attempt was made to determine the rôle that stimulation of the accelerator nerves might play in the effects of ether. A dog (B_2) was given 10 mg. morphine sulphate per kg. intramuscularly and within fifteen minutes there was complete A-V block. Epinephrin, 0.023 mg. per kg. in a 1-10,000 solution injected intravenously, increased somewhat the rate of the ventricle, changed the shape of the idioventricular groups, but had no influence upon the A-V block. Ether inhalation promptly abolished the block and accelerated the sinus rate. A phenomenon similar to that seen in the fourth experiment occurred during the early period of ether inhalation—an increase in the sinus rate with further impairment of conduction.

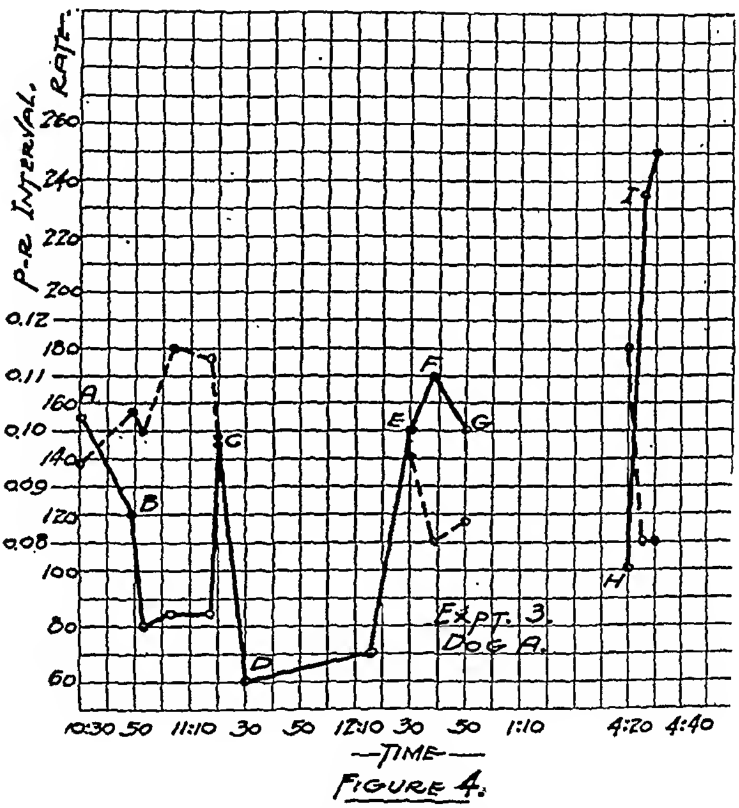

Fig. 4.—*A*, Control; *B*, one minute after 1 mg. morphine sulphate per kg. intravenously; *C*, two minutes after 2 mg. morphine sulphate per kg. intravenously; *D*, complete A-V dissociation; *E*, three minutes after starting inhalation of ether, light anesthesia, some struggling; *F* and *G*, deep ether anesthesia; *H*, completely recovered from ether anesthesia; *I*, one minute after 5 mg. atropine sulphate per kg. intravenously.

With the recovery from the ether, the vagal effects began to reappear. This experiment shows that the effects of the ether in all probability do not depend upon stimulation of the accelerators. (See Figs. 6 and 7.)

DISCUSSION

Ether is commonly employed for anesthesia in the study of the actions of drugs upon animals, and little attention is generally paid to

the possibility that these actions may be modified to an important degree by the anesthetic. Ether causes acceleration of the heart rate in the normal dog, and it has been shown that in the ordinary course of anesthetization by inhalation, it frequently produces changes in the cardiac mechanism seen in the electrocardiograms of animals[1] and man.[2] Eyster and Meek[3] and Cohn[4] observed that ether anesthesia frequently abolishes the arrhythmia produced by morphine. It has been reported that it diminishes the excitability of the vagus to elec-

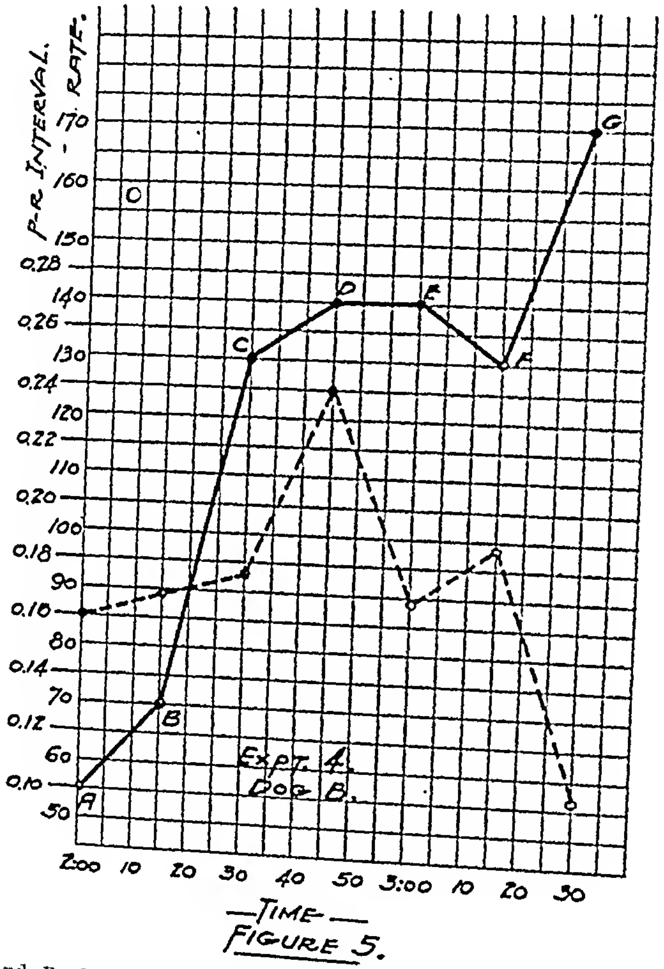

Fig. 5.—*A* and *B*, Controls, during morphine narcosis after 20 mg. morphine sulphate per kg. subcutaneously; *C*, three minutes after starting inhalation of ether; *D*, *E* and *F* deep ether anesthesia; *G*, two minutes after 0.3 mg. atropine sulphate per kg. intravenously.

trical stimulation. Thus Jackson and Ewing[5] found that ether raises and morphine lowers the threshold for the reflex of cardio-inhibition produced by electrical stimulation of the divided left vagus. They did not show whether the effect was central or peripheral. Ruttgers[6] found that after perfusing the frog's heart with 0.25 per cent ether, electrical stimulation of the vagus failed to produce slowing, and concluded that it paralyzes the endings of the vagus. There appears to be some evidence, however, that loss of response of the vagus mechan-

ism to electrical stimulation is not necessarily simultaneous with that to drugs. Witanowski[7] observed that when the frog's heart is perfused with a solution of ether, response of the vagus and accelerator to electrical stimulation disappears while that to acetyl choline and epinephrin is retained for some period.

In the present series of experiments the effect of ether upon the susceptibility of the vagus to stimulation by morphine was studied. The results uniformly show that ether anesthesia interferes with the action of morphine on the vagus in the heart. Within limits, the effect of ether and morphine are mutually antagonistic. Thus the effect of small doses of morphine may be completely abolished by the induction of ether anesthesia as seen in Experiment I, and the acceleration

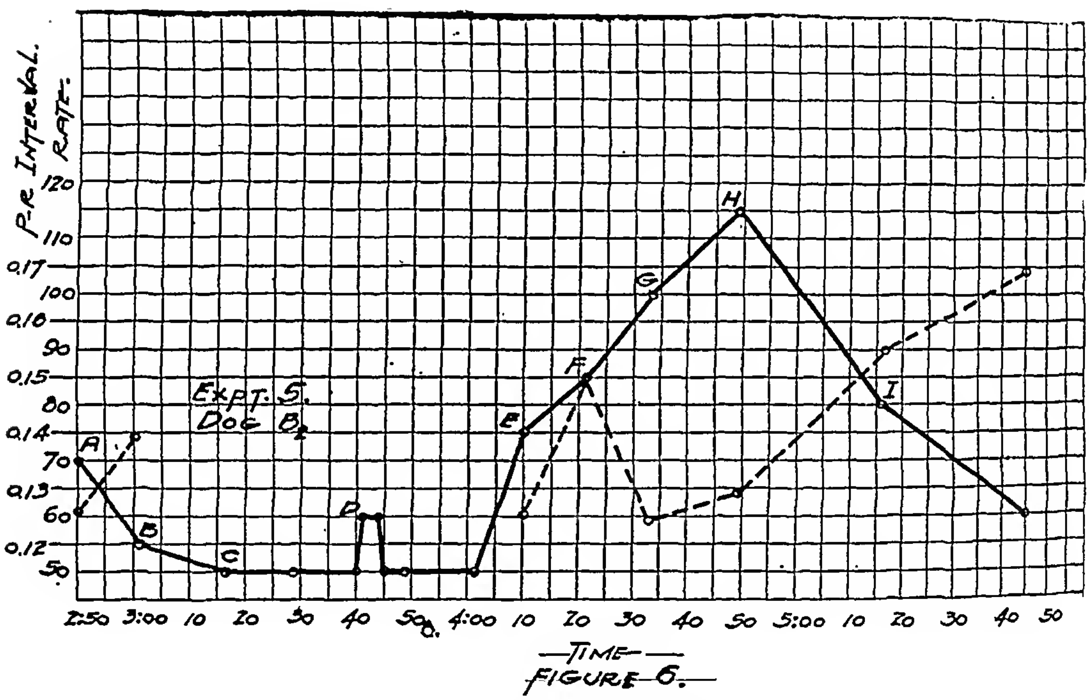

Fig. 6.—*A* and *B*, Controls; *C*, fifteen minutes after 10 mg. morphine sulphate per kg. intramuscularly, complete A-V dissociation; *D*, one minute after 0.023 mg. epinephrin 1-1000 per kg. intravenously; *E*, four minutes after starting inhalation of ether, slight struggling; *F* and *G*, deep ether anesthesia; *H*, fifteen minutes after ether discontinued; *I*, recovery from ether anesthesia.

of the heart during ether anesthesia may be overcome by a small dose of morphine as seen in Experiment II.

When ether inhalation was started, the animal often struggled violently, and it was thought that the effect attributed to ether may be due to stimulation of the accelerator nerves or reflex inhibition of the vagi as a result of the struggling. The fact that stimulation of the accelerators by epinephrin had no influence upon the morphine effect, whereas ether abolished the latter (see Experiment V) indicates that accelerator stimulation plays little, if any, part in the effect of the

ether, but that the latter effect is due to depression of the vagi. That it is not a reflex inhibition of the vagi, but in all probability a direct depression* of the center or endings by the anesthetic is apparent

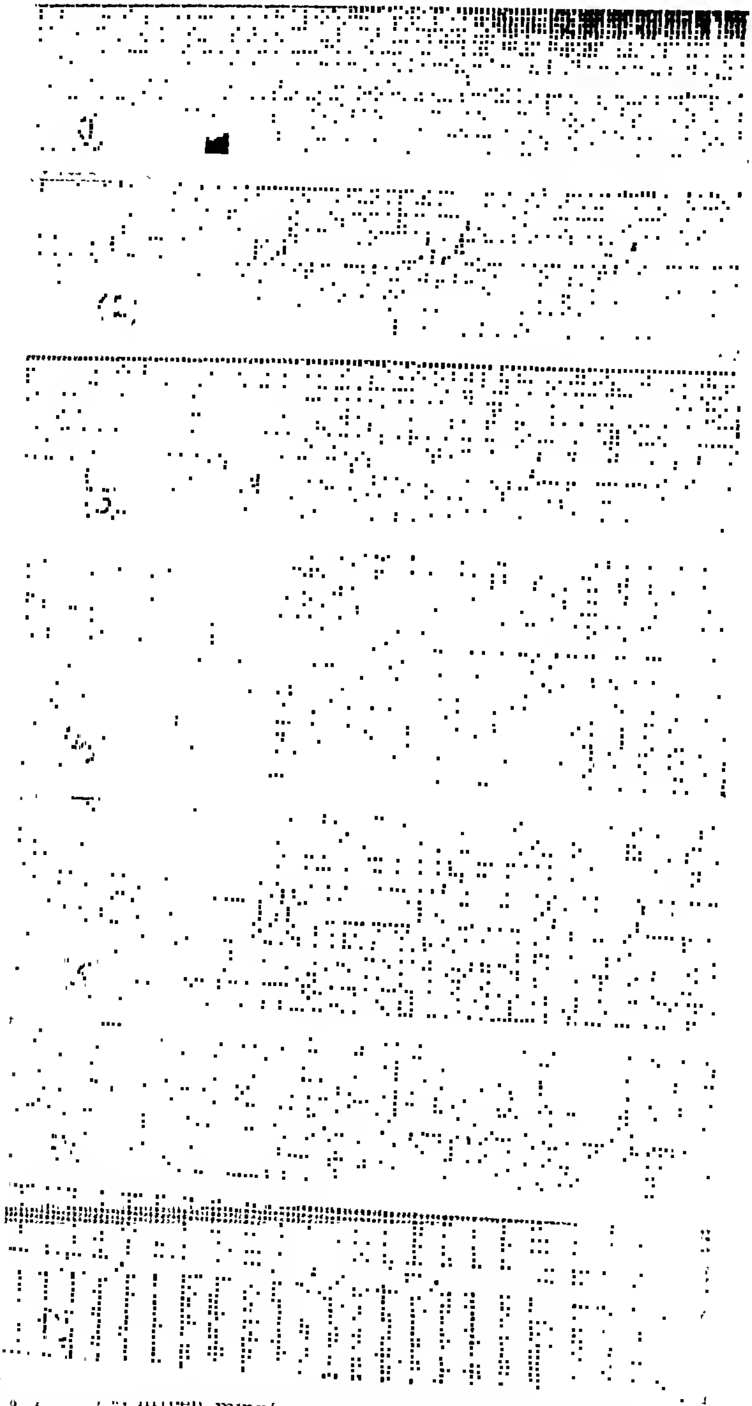

Fig. 7.—1 [illegible] fifteen minutes after 10 mg. morphine sulphate per kg. intramuscularly; 3, two minutes after 0.023 mg. epinephrin per kg. intravenously; 4, four minutes after the epinephrin; 5, four minutes after starting inhalation of ether, light anesthesia; 6, deep ether anesthesia; 7, seventy-one minutes after ether discontinued.

from several experiments in which the animal, somewhat depressed by the morphine, did not struggle when ether was administered and

*Reflexes may contribute to the inhibition of the vagus, especially if the animal struggles.

a considerable quantity of ether was inhaled before there was any acceleration of the sinus rate or shortening of the P-R interval.

Ether depresses but does not paralyze the vagi in the heart in any doses that do not paralyze respiration. Atropine, after the full ether effects have appeared, causes further acceleration of the rate and shortening of the P-R interval.

The effects of morphine on the heart vary considerably in different animals. Cohn[4] presented evidence indicating that some of these differences depend upon the fact that in one, the predominant effect is that of right vagus stimulation (marked sinus slowing); in another, the predominant effect is that of left vagus stimulation (marked disturbances in A-V conduction). On this basis it may be stated that ether usually depresses both nerves so that the rate is accelerated and conduction time is shortened. However, under given conditions, depression of the right vagus may be more in evidence than that of the left, as seen in Experiment IV, in which ether doubled the sinus rate but did not shorten the long P-R interval. This result probably depends upon the fact that after a large dose of morphine it requires much less ether to induce deep narcosis and the concentration of ether thus attained is insufficient to depress both vagi.

The initial lengthening of the P-R interval during ether anesthesia in this latter experiment, as also in Experiment V, is difficult to explain. That the sudden increase in the heart rate in the presence of impaired conduction might further depress conduction suggested itself as a possibility, but this explanation was refuted by the observation that after atropine, when the rate increased even further (from 140 to 170 a minute) the P-R interval shortened from 0.182 to 0.102 second. There are other possibilities, however, for which no evidence has been presented in this study, such as temporary local asphyxial changes affecting conduction, or that preceding the depression, there is brief stimulation of one vagus nerve, in evidence when its excitability has been greatly increased by a large dose of morphine.

SUMMARY AND CONCLUSIONS

1. Experiments were performed to study the effects of ether on the susceptibility of the cardio-inhibitory nerves to stimulation by morphine in the dog.

2. The results show that ether depresses the vagus and may abolish partially or completely the effects of stimulation of these nerves by morphine.

3. After large doses of morphine, deep ether narcosis may abolish vagus effects upon the sinus and not those upon conduction.

4. Ether by inhalation, in doses that do not paralyze respiration, depresses, but does not completely paralyze the vagi. Atropine is still effective after the full effects of ether have been induced.

5. Caution is necessary in the interpretation of the results of studies on the response of the vagus nerves in the dog during ether anesthesia.

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THE EFFECT OF OBSTRUCTION OF CORONARY ARTERIES UPON THE T-WAVE OF THE ELECTROCARDIOGRAM*

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THE T-wave of the electrocardiogram changes its form or direction when the myocardium is injured. This fact was observed experimentally by Eppinger and Rothberger[1] in 1909 and has had abundant confirmation in the human electrocardiogram. Eppinger and Rothberger further observed that the changes in the T-wave they induced tended to be opposite in character for the two ventricles. The injection of silver nitrate solution into the muscle of the right and basal portions of the heart caused the T-wave to become negative, whereas such injection into the left and apical portions of the heart resulted in a positive T-wave. They further found that spraying ethyl chloride on the heart also affected the T-wave, but the changes were opposite in direction to those following the injections. The effect of cold was confirmed by Wilson and Herrmann[2] and by Smith,[3] and the experiments of Wilson and Finch[4] indicate that the human heart responds in a similar manner.

I have previously shown[5] that the ligation of the right coronary artery causes negativity of the T-wave while ligation of arteries supplying the left side of the heart has the reverse effect upon the T-wave of the electrocardiogram. Since these effects are similar to those observed by Eppinger and Rothberger,[1] they are probably due to similar causes, as it is functional impairment of a given area of muscle which produces the changes in the electrocardiogram when coronary arteries are closed.

A re-investigation of the effect of cold was made,[6] and it was found that cooling the muscle, which prolongs the contraction, produced the effect reported by Eppinger and Rothberger, Wilson and Herrmann, and Smith; on the other hand, freezing the same areas of muscle so that their function was entirely abolished reversed the effect upon the T-wave. The facts suggest, therefore, the hypothesis that a tendency to negativity of the T-wave results from activity that is greater in duration or intensity in the muscle of the left lower portion of the heart, which may be actual or relative as a result of diminished activity in its antipode, the right upper portion of the heart. When the positive influence upon the T-wave is considered the circumstances are reversed.

Rothberger and Winterberg[7] in 1910 observed that the activity of the accelerator nerves very markedly influences the T-wave of the elec-

*From the Laboratory of Physiology, Faculty of Medicine, Paris.

trocardiogram and that a distinct form is associated with the stimulation of each nerve. I[8] have recently reported that the stimulation of the right accelerator nerve is often associated with a negative influence upon the T-wave, and the stimulation of the left accelerator nerve with a positive influence upon the T-wave—effects which are similar to those caused by injection of the muscle[1] or the closure of coronary arteries.[5] If the above hypothesis is correct, accelerator nerve stimulation affects the T-wave of the electrocardiogram by decreasing the duration of the activity of the muscle affected.

Similar changes in the T-wave are also obtained by changes in the intracardiac pressure.[9] A sudden increase in the intracardiac pressure of the right ventricle (clamping the pulmonary artery) causes temporary negativity of the T-wave and the same procedure in the case of left ventricle (clamping the aorta) tends to produce the reverse effect. Here the T-wave is affected perhaps because interference with the function of the muscle upon the side in which the intracardiac pressure is increased results in relatively greater function in the muscle of the antipode.

This report is concerned with the changes in the T-wave of the electrocardiogram when the three principal vessels of the heart (the right coronary artery, and the circumflex and anterior divisions of the left coronary artery) are obstructed. These vessels supply respectively the right upper and anterior, the left posterior and lower, and the intermediary or apical portions of the heart. The experiments, therefore, were actually determining the effect upon the electrocardiogram of interference with the function of large areas of muscle in these three portions of a heart.

The experiments were upon dogs under chloretone narcosis, with artificial respiration and the heart exposed by removing the sternum. The electrocardiograms were taken with the electrodes inserted into the right forepaw and left hind leg. There were eighteen experiments in all. In four, the mechanical movements of the heart were simultaneously registered from the base of the right ventricle after fixing the apex to the diaphragm with a single suture. In every instance the artery was obstructed by gently lifting it from its bed and applying a small clamp. The discoloration and loss of muscle function which follow[10] occurred promptly. With the removal of the clamp the color and function of the muscle were rapidly restored and the electrocardiogram returned to the original form. The clamp was not applied longer than three minutes.

It has been pointed out by Lewis[10] that the first changes in the rhythm of the heartbeat occur after a considerable interval following coronary obstruction. In these experiments there was no change in rhythm during the three-minute periods of occlusion.

The closure of the right coronary artery had a negative influence upon the T-wave of the electrocardiogram. The closure of the circumflex division of the left coronary artery had the opposite effect, namely, elevation of the T-wave. The closure of the anterior division of the left coronary artery tended to produce both effects, i.e., the T-wave began before the complete ascent of S, yet its peak became more positive. In two of the experiments the closure of this vessel caused only the positive effect upon the T-wave. These effects are shown in Fig. 1.

The zone of discoloration which followed the closure of the anterior division of the left coronary artery appeared at the lower portion of

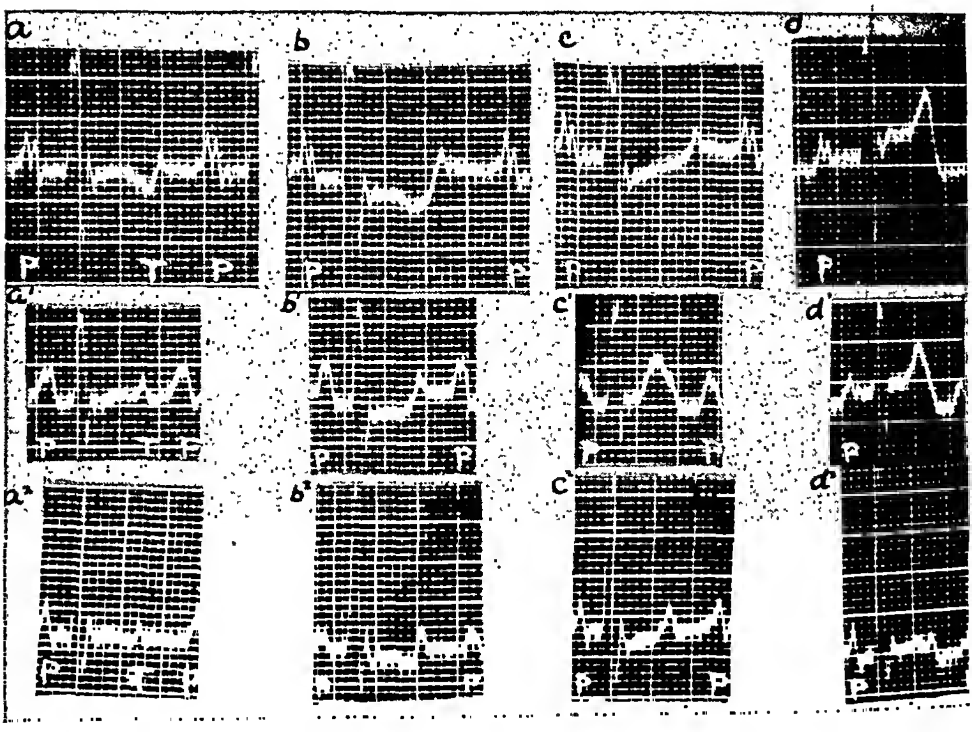

Fig. 1.—Axial electrocardiogram. Time in fiftieth seconds. *a*, The normal; *b*, closure of the right coronary artery; *c*, closure of the descending division of the left coronary artery; *d*, closure of the circumflex division of the left artery. a^1 b^1 c^1 d^1, The same, another experiment. In this animal only the positive influence on the T-wave from the closure of the descending division of the left artery appeared. a^2 b^2 c^2 d^2, The same, a third experiment. The small degree to which change occurred here was not due to an equivalent insignificance in the changes occurring in the muscle. The latter was as prominent as in other experiments.

the anterior interventricular groove and the apex of the heart. Dividing the ventricles into two halves, the one to the right above and anterior, the other to the left and posterior, it was, roughly, between the two. The involvement in the portion of the heart situated on its right side tended to cause negativity of the T-wave and involvement in the portion on its left side positivity of the T-wave. The expectation, therefore, that the closure of the anterior division of the left coronary artery would produce less characteristic change in the form

of the T-wave than would be the case with the other two vessels, and that the change which occurred would partake of the nature of that associated with the closure of one or both of the other two was fulfilled.

In three of the experiments, immediately after the closure of the circumflex division of the left artery, the T-wave became negative before the usual effect, positivity of the T-wave, appeared (Fig. 2). This fleeting reversal of the effect upon the T-wave is similar to that which is often observed when the accelerator nerves are stimulated.[8]

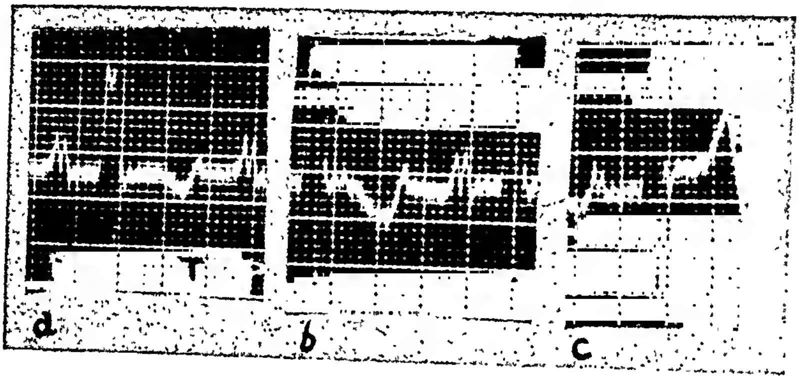

Fig. 2.—Axial electrocardiogram. Time in fiftieth seconds. *a*, Normal; *b*, the earlier effect of the closure of the circumflex divisions of the left coronary artery, which passed quickly into *c*, the enduring effect.

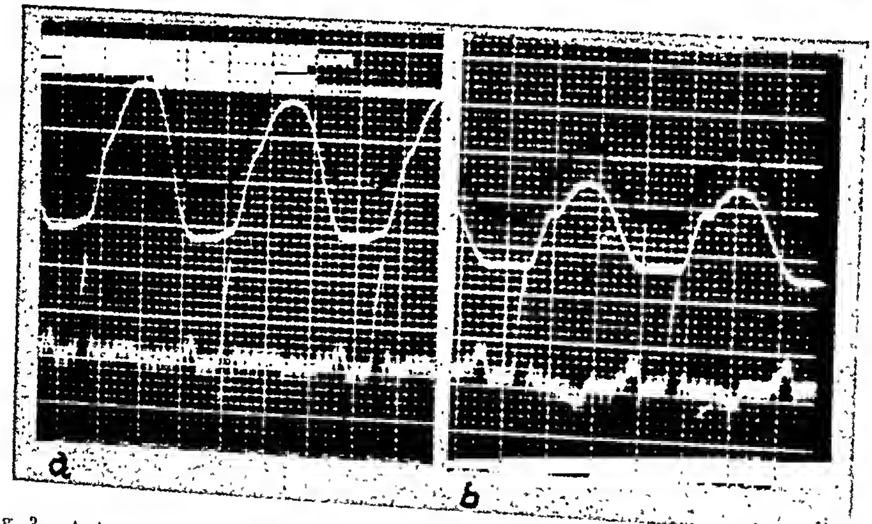

Fig. 3.—Axial electrocardiogram with mechanocardiogram. *a*, Normal; *b*, closure of the right coronary artery. The electrocardiogram presented little change, although the mechanocardiogram indicated there was marked diminution in the activity of the right ventricle.

There was no relation between the degree to which the T-wave was altered and the relative size of the area of the myocardium involved. With extensive involvement of the myocardium the resulting electrocardiographic changes may be insignificant. In Fig. 3 the effect upon the mechanocardiogram and the electrocardiogram is seen after the right coronary artery was clamped. Closing the lumen of this vessel

impairs the function of a large portion of the outer wall of the right ventricle. This experiment presented an unusual contrast between the two because the change in the T-wave was insignificant.

SUMMARY AND DISCUSSION

The experimental occlusion of the principal coronary arteries produces changes in the T-wave of the electrocardiogram which vary in direction depending upon the vessel involved. When the muscle of the right and anterior portions of the heart (including the basal portion in that region) is involved by the occlusion, the T-wave tends to become negative, and when the muscle of the left and posterior portions of the heart is involved, the reverse is the case; the T-wave tends to become positive. These and other observations cited suggest that the T-wave of the electrocardiogram *of the intact heart in situ** reflects the disturbances which occur in the balance of the electrical activity of the two halves of the heart (the halves correspond approximately to the right and left ventricles). When a change in the heart muscle occurs, the effect that is exerted upon the T-wave depends upon the location of the injury with respect to the two halves of the heart.

The axial lead was employed for these experiments. That the line of the leading also plays an important rôle in the form of the T-wave is suggested by the work of Katz and Weinman.[11] These authors concluded, however, that the T-wave is due to an unequal duration of the activity of the various fractions of the ventricles. Further evidence is visible in the fact that the curves of simple strips of heart muscle,[12, 13] electrograms, do not essentially differ from curves of the entire heart, electrocardiograms. I have called attention[14] to the influence that the line of the lead may have in determining the form of the T-wave after the stimulation of the accelerator nerves.

Further investigations along these lines will be reported in subsequent communications.

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*The view is not concerned with the factors which cause the changes in the T-wave of the electrogram.

MYXEDEMA HEART*

With Report of Two Cases

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THE so-called myxedema heart was first recognized by Zondek[1] in 1918. As characteristic features he described the marked enlargement of the left and right ventricles of the heart, slow pulse rate, normal blood pressure, and electrocardiographic changes.

In his first paper, Zondek reported four cases of myxedema which showed the classical features of the disease, and in which the teleroentgenograms revealed an enlargement of the heart both to the right and to the left, with a marked reduction in its transverse diameter after thyroid therapy. The electrocardiograms of his patients showed low or absent P-waves, absent T-waves, and changes in the QRS complexes. The intraventricular conduction defects disappeared with the reduction in the size of the heart when thyroid extract was administered. As these patients improved, the basal metabolic rates increased.

The transverse cardiac diameter in Zondek's first case measured 19.7 cm. In order to test whether this "high grade dilatation is in reality an expression of the myxedematous syndrome," he studied the influence of thyroid substance on the size of the heart. After four weeks of this therapy, there was a definite reduction in size; the transverse diameter now measured 17.8 cm. Eight weeks after the beginning of treatment, there was a still more marked reduction, to 14 cm., which was the normal for that individual patient. The changes noted on fluoroscopy were that the heart appeared as a "lifeless, expressionless mass with deformed contour"; "a livelier action and normal cardiac silhouette were revealed" after therapy. The electrocardiograms also returned to normal. Corresponding changes were obtained in the hearts of the three other patients. The illustrations of Zondek's roentgenograms and electrocardiograms before and after treatment are very striking. Zondek thought that the marked reduction of the size of the myxedema heart suggested a specific effect, but the details of his theory will be discussed later in this paper.

Since his original observations, there have been few contributions to the subject of myxedema heart. Assmann[2] in 1919 reported a case confirming the findings of Zondek. Assmann's patient had a pulse rate of 50 beats per minute, a transverse cardiac diameter of 16.7 cm.; but following thyroidin, 0.3 gram daily for three weeks, the

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transverse diameter was reduced to 12.7 cm., and the pulse rate increased to between 70 and 80.

In his 1918 paper, Zondek showed that the myxedema heart resulted from the damage to the myocardium and not to the nervous elements of the heart and that the therapeutic influence of thyroid extract is on the muscle. In his second paper, published in 1919,[3] he reported two further cases. One, a sixty-two-year-old woman, showed mild signs of cardiac insufficiency and had a blood pressure of 160 mm. and a pulse rate of 52. The x-ray plate showed enormous dilatation of all the cardiac chambers and marked widening of the aorta. It is of particular interest to note that the electrocardiogram showed absent P- and T-waves. In addition, there were ventricular extrasystoles in which the T-waves were present. This brought up the question whether the muscle of the myxedema heart was in a state of diminished susceptibility to excitation or was of diminished contractile power. This was suggested because the extrasystolic contraction revealed the fact that the myxedema heart is capable of eliciting a T′-wave. It is not known whether the normal T-wave and the T′-wave of an extrasystole are due to one and the same phenomenon. His second case, a forty-two-year-old major, has frequently been quoted because of the unusual development of the disease in this patient. This man received a gun-shot wound in his neck which resulted in a long period of suppuration of the thyroid gland. He then developed typical signs of myxedema and cardiac insufficiency due to the presence of a myxedema heart, the symptoms of which began twelve months after the original injury. These findings were confirmed by x-ray films and electrocardiograms. The latter showed absent P- and T-waves. After three weeks of thyroid treatment, the symptoms of cardiac insufficiency had subsided and the transverse cardiac diameter had been reduced by 1 cm.

Meissner, in 1920,[4] reported three similar cases. The first was a patient of fifty-six years in whom there was marked cardiac enlargement to the left and right; the sounds were rough, the second apical sound was not accentuated. The pulse rate was 50. The teleroentgenogram showed a transverse diameter of 20 cm.; after treatment the measurement was reduced to 15.5 cm. A comparison of the findings in the x-ray plates before and after thyroidin is very striking, especially when one considers that myxedema had been present for twelve years. The second patient had a blood pressure of 180 mm. and a pulse rate of 58. Examination of the heart, blood pressure, and urine suggested a chronic nephritis, but the entire picture was decidedly in favor of myxedema. After two months administration of thyroid, there was a marked improvement of the patient's condition, the pulse rate now being 66 and the blood pressure 160 mm. systolic. It is very interesting, however, to note that the x-ray plate in this case showed no change in the size of the heart. The author interprets this lack

of reduction as due to a complicating chronic nephritis. This, he states, may explain the failure of the influence of thyroid substance on the size of the heart. The third case showed a normal heart before thyroid extract was administered and no change in the cardiovascular system afterwards. Thus only the first case in this report resembles the typical ones of Zondek.

It was not until 1925 that the first paper dealing directly with myxedema heart appeared in this country. This was a communication by George Fahr[5] who emphasized the rarity of the condition and stated that he was able to collect only eight cases in the literature up to that time. He further stated that he had seen three cases in one year. There has been a moderate amount written in the American literature concerning observations on the heart in myxedema, but very few authors have published x-ray and electrocardiographic reports.

Fahr's first case was typical myxedema in a woman of forty-six years who had all the signs of cardiac insufficiency. The pulse was 70, blood pressure 110/70 mm.; and the basal metabolic rate was minus 25 per cent. The teleroentgenogram showed right and left cardiac enlargement, with a transverse diameter of 17 cm. This patient was given rest in bed and tincture of digitalis for three weeks. Under this régime there was very little improvement in the edema, dyspnea, and other cardiac complaints. Digitalis was then stopped and eight grains of thyroid extract were administered each day. A marked improvement in the cardiac condition resulted, so that seven weeks later the transverse cardiac diameter was 14.5 cm. At this time the basal metabolism was plus 8 per cent, the pulse rate 80, and the blood pressure 120/80 mm. This author controlled his results by a therapeutic test. He discontinued the thyroid medication, and there was a return of all the signs of myxedema, including those of cardiac insufficiency. The metabolism rate diminished and the teleroentgenogram proved that the heart had again enlarged, its diameter was then 15 cm. Medication with thyroid extract was resumed, and six weeks later the signs of myxedema again disappeared, the basal metabolic rate increased, and the heart became normal in size. Parallel findings were noted in the electrocardiograms. On admission there was an intraventricular block with negative T-waves in Leads I and II; the ventricular complexes were negative in Lead III, and the P-waves were normal. After thyroid medication was tried, the electrocardiograms became normal, but when the medication was discontinued, the characteristic intraventricular conduction defects reappeared, with negative T-waves in Leads I and II. Fahr's second case showed mild symptoms of cardiac failure, with typical x-ray and electrocardiographic changes of myxedema heart, which returned to normal after treatment.

A further review of the American literature will be given following these two references to the French.

Laubry, Mussio-Fournier and Walser,[6] in 1924, reported a case of myxedema in a patient who complained of typical anginal attacks and who showed cardiac hypertrophy without valvular lesions. Digitalis and other remedies gave no relief, but when thyroid medication was tried, there was marked clinical improvement, with a corresponding reduction in the cardiac volume.

P. Abrami and his coworkers[7] reported two cases, in both of which the patients complained of precordial pain. These authors do not present a very careful, detailed study of their cases and do not report the electrocardiograms. One is not convinced that they were actually dealing with myxedema heart, but one gets the impression that their cases were probably instances of coronary thrombosis.

Christian in 1925[8] stated that although he had seen thirty-two cases of myxedema at the Peter Bent Brigham Hospital, he had not observed one case like those described by Fahr, and suggests the rarity of the myxedema heart. Sturgis,[9] in his paper entitled: "The Treatment and Prognosis in Myxedema," a study based upon twenty-six patients, refers to Fahr's article and states that in this disease, serious impairment of the myocardium is amenable to thyroid medication. He discusses at length the therapy in these cases, but he does not report any definite cases of myxedema heart which resemble those of Zondek, Assmann, or Fahr. This same writer in 1926[10] reported a case in a woman of fifty years, who had myxedema and who also complained of anginal attacks. The basal metabolic rate of this patient was minus 32 per cent and her blood pressure was 135/110 mm. On clinical examination the left border of the heart was 9.5 cm., and the right border 3.5 cm., from the midsternal line. He did not mention the electrocardiogram or x-ray findings. In another case of myxedema in a man of fifty-seven, who complained of dyspnea and substernal oppression, the basal metabolism was minus 37 per cent. The teleroentgenogram showed "uniform and rather striking enlargement of all four chambers of the heart." Thyroid extract was administered, but the patient still complained of substernal pain on slight exertion. No note was made concerning the x-ray result after treatment, nor did he mention any reduction in the size of the heart. Electrocardiographic reports were also omitted. It is possible that the cardiac enlargement in this case may have been due to a hypertension and not to a primary dilatation. Sturgis again wrote on the cardiovascular system in myxedema in 1927.[11]

Willius and Haines[12] studied 162 cases of myxedema with particular reference to the cardiovascular system. Eleven cases, or 7 per cent, showed evidences of cardiovascular damage, such as cardiac hypertrophy and myocardial insufficiency associated with hyperten-

sion, renal disease, arteriosclerosis, or angina pectoris. In one man of forty-eight years, who complained of dyspnea and extreme weakness, a moderate cardiac hypertrophy with bradycardia was found. The electrocardiogram gave evidence of prolongation and notching of the QRS complexes in all leads. These findings disappeared after thyroid extract was given. These authors found no change in the size of the heart, but they did not publish the teleroentgenograms. "Subsequently, the T-waves in Lead II and III became negative, increasing the probability of the associated degenerative myocardial changes." Here, again, it is questionable whether this case is a true myxedema heart. Electrocardiographic studies were made in 55 of their cases; 28 of which were found normal; in 12 the results were incomplete; in 12 others the abnormalities disappeared after thyroid administration. From their data they conclude that a cardiac syndrome of myxedema does not exist.

Means, White, and Krantz[13] collected 48 cases from the Massachusetts General Hospital where they looked particularly for the cardiac changes in myxedema. They report one case in which the cardiac enlargement subsided when thyroid substance was given. This was a woman of forty-four years, a typical myxedema patient, in whom the basal metabolism rate was minus 34 per cent, the pulse rate 66, and the blood pressure 148/90 mm. The electrocardiogram was normal. The seven foot plate of the heart revealed a general enlargement, with a transverse diameter of 14 cm. This patient was given thyroid extract and fifteen days later, the basal metabolic rate rose to minus 4 per cent and the x-ray plate showed a transverse cardiac measurement of 11.7 cm. The pulse rate rose to 100 per minute. Incidentally, this patient died suddenly sixteen days later. These authors believe that the condition of myxedema heart exists, but that it is exceedingly rare.

Curschmann, in 1926,[14] reported a case of myxedema heart in a man sixty years old, with results similar to those of Zondek and Meissner. In a woman of forty-seven with myxedema heart and cardiac insufficiency, Zins and Rösler[15] showed a reduction of the transverse cardiac diameter from 14.9 cm. to 11.6 cm. after three weeks of thyroidin.

Another case report was published recently by Schittenhelm and Eisler.[16] The basal metabolism rate was minus 20 per cent, the blood pressure 150/96 mm., and the pulse rate between 60 and 70. They reproduced the x-ray plate, which demonstrated a marked cardiac enlargement to the right and left, the transverse diameter measuring 18 cm. The electrocardiogram showed a small P-wave, negative T-wave, and small waves in the first and second leads. They administered 12 mg. of thyroxin intravenously in eleven days. They then demonstrated a reduction in the transverse cardiac diameter to 14.7 cm. and a normal electrocardiogram.

In 1927 Fahr[17] reported six cases of myxedema heart including the first case reported in his earlier paper.

Because of the scarcity of case histories in the study of myxedema heart, the following two cases of myxedema, with the typical roentgenographic findings, seem of sufficient interest to report. The first patient was studied on the medical service of Doctor B. S. Oppenheimer, to whom I am greatly indebted for the privilege of reporting the findings.

Fig. 1.—Appearance of the patient, L. S. (Case 1), before thyroid extract was given. Note the expressionless face, the thick lips, and the pigmented dorsal surface of the hands.

Case 1.—L. S., aged fifty-eight years, who had been married for thirty years, had four living children. He was known to have had myxedema for eighteen years, but he had never adhered strictly to treatment and had never been studied in any one clinic. He showed the characteristic slow mental reactions and other features of the disease. When first seen, he took very little interest in his environment, was very uncooperative and refused to answer direct questions. Typical answers in his history are: "I don't care," and "What difference does it make?" He was once a painter, but had not worked for years because he felt "sick and weak." He always complained of feeling cold, seldom shaved, and had not had his hair cut

in two years. Examination revealed an expressionless face, thick lips, diminished palpebral fissures, pads of thick tissue about the eyes and supraclavicular swellings. He passed most of the days in sleep and seldom left his bed. Other classical features, such as dry skin, irregular borders of the hair distribution, and slow, sluggish speech were noted. There was an abscence of axillary hair and scanty pubic hair. The tongue was thick and pudgy. The thyroid gland was not palpable. Examination of the heart showed that it was enlarged. The pulses were equal, regular, of fair tension, and rate of about 66 per minute. On palpation no demonstrable thickening of the peripheral vessels could be detected. The blood pressure was 110/68 mm. There was dullness over the right lower lobe of the lung and a few crepitant râles were heard. The hands and feet were short, and the skin was thickened. The scrotum showed patches of vitiligo. The dorsal surfaces of the hands revealed a roughened, scaly, brown pigmented skin. Examination of the blood revealed a moderate secondary anemia. The basal metabolic rate before treatment was minus 20 per cent. The urine contained no albumin

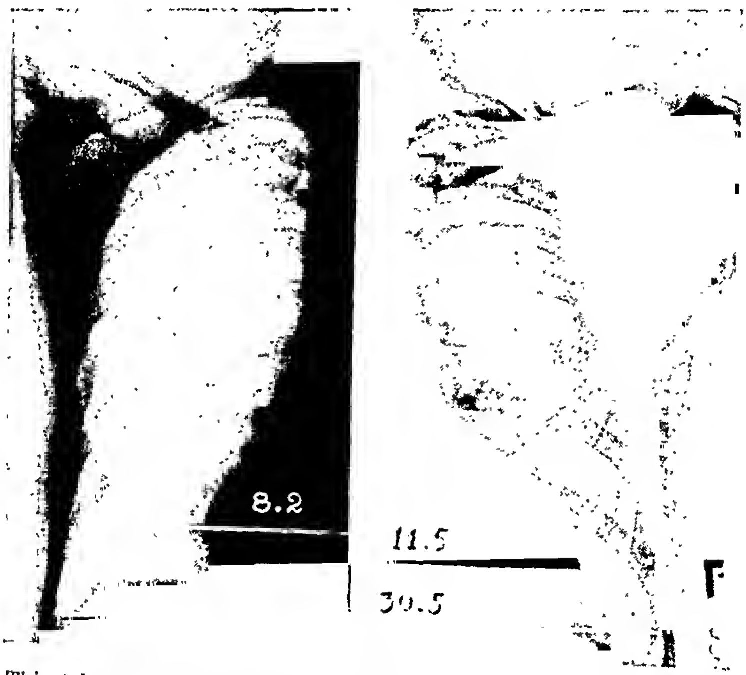

Fig. 2.—This teleroentgenogram shows the dilatation of the heart involving chiefly the right and left ventricles. The transverse diameter measures 19.7 cm. This plate was taken shortly after his hospital admission. The pneumonic process at both bases is not well reproduced.

or casts; the phenolsulphonephthalein output was 65 per cent in two hours; and the kidney showed good concentrating power. The blood chemistry was as follows: urea nitrogen 18 mg., cholesterol 258 mg., calcium 9.6 mg., and blood sugar 98 mg. He refused to have a Janney test performed. The blood Wassermann was negative. He weighed 152 pounds. The temperature was usually around 98 degrees F. Fig. 1 shows the appearance of the patient during the first few days of his admission to the ward.

Before ordering thyroid medication, the teleroentgenogram was taken. It showed (Fig. 2) a moderate dilatation of the left ventricle and a marked enlargement of the heart to the right. There were the remains of a pneumonic process at both bases of the lungs. The electrocardiogram taken at this time showed low voltage in all three leads, a left ventricular preponderance, notching and prolongation of the QRS complexes in all leads (their interval was prolonged to 0.12 seconds), and flattening of the T-waves in Lead III (Fig. 3). The patient was

put on thyroid extract, six grains per day, and shortly afterward, he showed the usual dramatic improvement. He became more alert; began to feel warm for the first time in years, and asked to get out of bed. The basal metabolism rate gradually rose, so that on the tenth day it was minus 12 per cent. An x-ray plate taken three weeks later showed a disappearance of the inflammatory process at the bases but no change in the size of the heart. Thyroid extract was continued until a total of 173 grains had been given in seven weeks. At this time the patient's pulse became more rapid; there was a marked improvement in his mental attitude and alertness. He began to take an interest in his person, and shaved twice a week. His blood pressure was 108/64 mm. He felt so much bet-

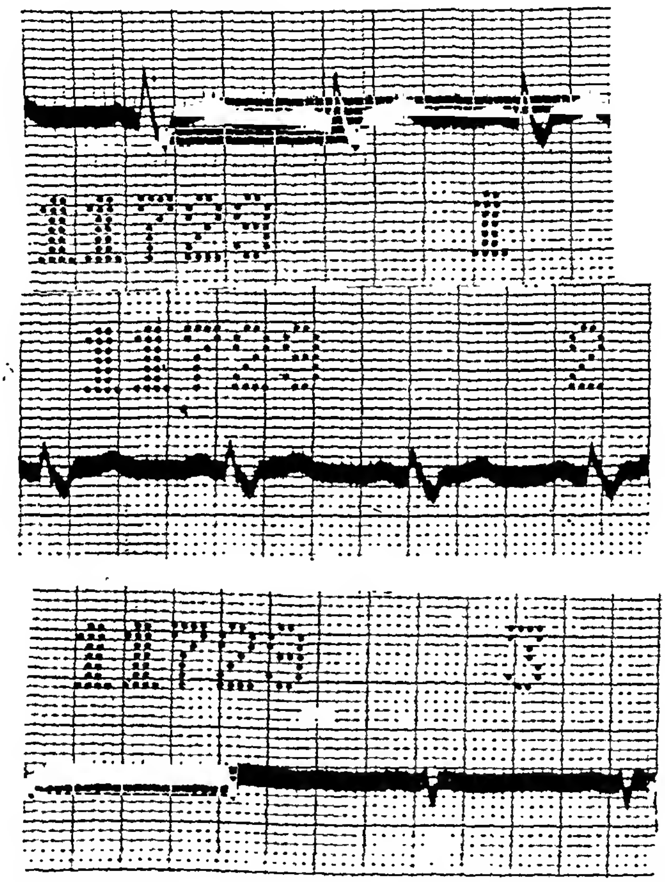

Fig. 3.—Three leads of the first electrocardiogram before treatment are shown. See text for description.

ter that he was discharged. At this time his basal metabolism was plus 9 per cent. Another x-ray was taken which revealed no change in the size of the heart. Another electrocardiogram showed even better than the previous one the notching of the QRS in all three leads, the low voltage in all leads, the inversion of the T-wave in Lead III, and an intraventricular conduction defect.

After discharge the patient was given maintenance doses of thyroid extract and was seen at intervals of two weeks. He claimed to have adhered to his therapy regularly. There was such a marked improvement that he said his own friends did not recognize him. Two months later a seven-foot plate of his heart showed no demonstrable reduction in size (Fig. 4). The apparent difference in the transverse diameter could well be explained, according to the interpretation of Dr. Harry Wessler, as resulting from changes in the height of the diaphragm which

occur during the respiratory cycle. Variations in the technic of taking the plates may account for slight changes heretofore reported in the literature. His basal metabolic rate now was minus 4 per cent, his pulse rate 70. He did not complain of any feelings of discomfort. An electrocardiogram taken two months after treatment also revealed no definite changes as compared with those taken earlier.

One of the most striking features in this case is the absence of reduction in the size of the heart and of improvement in the electrocardiographic changes, despite thyroid administration which was otherwise efficacious. There is a marked contrast between those cases of myxedema in which the electrocardiographic and roentgenological abnormalities disappear after thyroid medication (Zondek, Assmann, and Fahr) and those, like the case just cited, in which no definite

Fig. 4.—The result after two months of thyroid therapy. Although there is an apparent reduction in the transverse cardiac diameter (18 cm.), this may be due to differences in the height of the diaphragm.

changes could be demonstrated. One may conclude that in myxedema the cardiac manifestations fall into two groups: In one are those cases in which the administration of thyroid extract results in reduction of the cardiac size and a disappearance of the abnormalities in the electrocardiogram. In the second group one may consider those cases of myxedema in which the roentgenological and electrocardiographic evidences point to cardiac changes, but wherein one can find no amelioration after a sufficient course of thyroid extract.

In a personal communication to the author, Zondek stated that he has seen two such cases as the one reported in this paper, in which the cardiac manifestations did not return to normal after thyroid therapy. This suggests a definite organic myocardial change in the

latter group, not amenable to the influence of thyroid medication. Case 1 resembles the second case of Meissner, already quoted, where similar observations were made. It is possible that the long duration of myxedema (over eighteen years) may have been a factor in the production of organic changes in the heart; changes of such a character that they could not respond to thyroid therapy. These observations may be of further help in establishing the mechanism of the reduction in the size of myxedema heart in such cases as those quoted by Zondek. He stated that the apparent enlargement of the myxedema heart was due to a dilatation, because of the rapid reduction in size in response to thyroid. The characteristic cases in the literature show that when reduction occurred, it usually took place within a few weeks. The

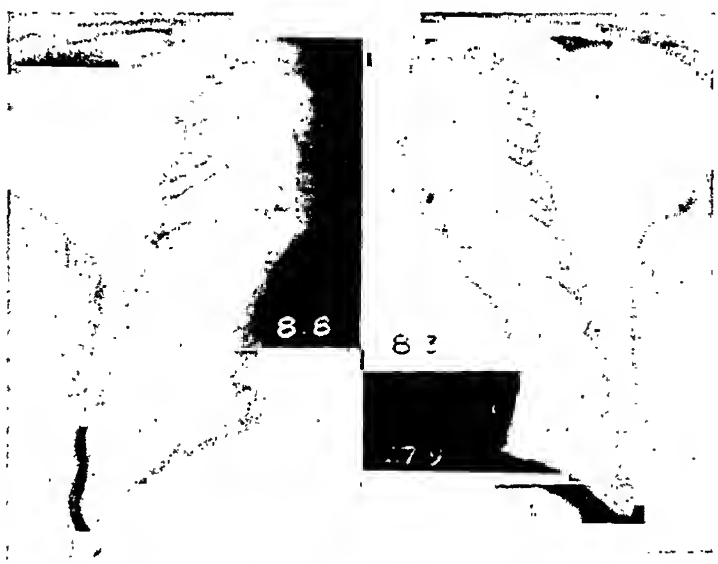

Fig. 5.—Teleroentgenogram of Case 2 (M. H.). There was a general enlargement of the cardiac shadow to the right and left.

case presented in this report was observed for over four months. No further changes in the size of the heart may be expected. This we interpret as an expression of cardiac hypertrophy *per se* and would expect to find, histologically, fibrosis of the myocardium.

Case 2.—M. R., twenty-six years old, male, single, was studied in the dispensary service of Dr. Harry Wessler. This patient had always been a "good student," but was very phlegmatic and could never hold any responsible position. He complained of "inability to work." On examination, the puffiness of his eyelids and the thick, broad tongue were prominent features. On percussion the heart was enlarged to the left. There was a moderate pretibial edema, a palpable liver, and an enlarged spleen. The nonprotein nitrogen was 35 mg., the blood cholesterol 200 mg. The total protein and differential blood picture were normal. The blood volume was found to be 3.1 or 50 c.c. per kilo. The initial basal metabolic rate was minus 18 per cent. The patient weighed 139 pounds, his blood pressure was 100/60 mm., urine was negative.

X-ray films of the skull were negative. A teleroentgenogram (Fig. 5) showed a "marked enlargement" of the heart. "It is globular in shape and under the fluoroscope the cardiac contractions were seen to be very poor." The electrocardiogram revealed a tendency toward a left ventricular preponderance.

ELECTROCARDIOGRAPHIC CHANGES

There have been many electrocardiographic studies in thyroid insufficiency. Some of the findings have already been quoted. Zondek[1] originally observed low P- and T-waves. He thought that electrocardiograms were the best guides to therapy and suggested their use in control.[18] It is difficult to explain why the P- and T-waves are absent and return after treatment.

Zondek[19] stated that there is a different underlying condition to explain the diminished action and power of the myxedema heart from that in myocardial insufficiency due to other causes. He thinks that the return of the T-waves after treatment is due to a gradually increasing strength of the heart's action. By means of phlebograms[19, 20] he demonstrated that the auricular wave is absent in this disease. The auricle, however, is not "still"; a number of minute twitchings are shown, which may be due to an "auricular tachycardia." The dilatation of the auricle is passive, the so-called myogenic dilatation due to stasis. There is a diminution, consequently, in the propulsive force of the heart. Thus he explains the absence of P-wave. The subsequent work of Lueg[25] and of Nobel, Rosenblüth and Samet[23] offer a better explanation.

Thacher[21] studied electrocardiograms of 8 cretins and concluded that the T-wave is flattened, low, or even inverted in cretinism and returns to the normal after thyroid administration.

Gardner[22] reported a case in which there was a splitting and widening of the QRS complex and negative T-wave in Lead I with a return to normal after giving thyroid extract. Nobel, Rosenblüth, and Samet[23] also studied the electrocardiograms in thyroid insufficiency and came to similar conclusions. Thacher and White[24] showed in every one of 14 cases of myxedema, a decrease in the height of the T-wave in Lead I as compared with the normal. No auriculo-ventricular or intraventricular block was noted. The P-R interval was usually normal. The QRS complexes in some cases showed a decreased amplitude and "increased as did the T-wave with thyroid." These authors draw a definite relation between the T-wave as observed in the electrocardiogram and the basal metabolic rate in myxedema.

Fahr does not agree wth Zondek that the P-wave is necessarily absent in the electrocardiograms of the myxedema heart, because it was practically normal in his cases. He is of the opinion that a negative T-wave in Leads I and II is the most characteristic change in the electrocardiogram and that the QRS changes are less common. In his

first case, the first change to normal after the administration of thyroid extract was in the T-wave in Lead I, which was diphasic at first and later positive. Next the slurring of the QRS became normal and the conduction time decreased.

Lueg[25] attempted to explain the electrocardiographic changes in hypothyroidism by an altered electrical capacity of the skin rather than by myocardial changes.

Nobel, Rosenblüth and Samet state that the increased resistance of the skin and tissues could, in part, account for the changes in the electrocardiograms. To decide this question they investigated the skin resistance, which was known to be increased, and then attempted to reduce it. In place of the usual plate electrodes they substituted needle electrodes, both on the extremities and thorax. The resulting electrocardiograms taken by the new technic (employing one needle electrode in the sternal end of the second right intercostal space and the second needle in the region of the cardiac apex) revealed the presence of P- and T-waves. They concluded that there are no changes in the conductive mechanism of the myxedema heart, but that the electrocardiographic changes are expressions of the abnormal skin resistance and, therefore, an indirect evidence of metabolic changes. These conclusions speak against the theory of Zondek; namely, that the absence of P- and T-waves is due to a disordered cardiac conduction mechanism.

THYROID MEDICATION

Sturgis and Whiting[9] administer thyroid gland, 0.13 gm., three times a day for five days. The patient is carefully watched for such untoward signs as loss in weight, rapid pulse rate, and complaints of palpitation, dyspnea, dizziness, nausea, or a feeling of warmth. If these do not appear, they continue giving thyroid tablets, 0.13 gm., twice a day, continuing until the pulse is about 75. Maintenance doses of 0.13 gm. daily are given when a satisfactory basal metabolic rate has been reached.

These authors advise a careful watch for untoward signs, because some patients with myxedema have serious cardiac impairment. They report the case of a woman of fifty years (quoted above[10]) who died suddenly during her treatment. At post-mortem examination, coronary arteriosclerosis, cardiac infarction, and hypertrophy with dilatation were found. Christian sounds the same warning. These authors suggest that after thyroid treatment, the increase in the metabolism throws an added burden on an already damaged myocardium which is unable to meet the strain.

Zondek also warns against treating patients with thyroid extract without sufficient grounds. He thinks that in the absence of cardiac

enlargement and electrocardiographic evidences, care should be exercised in the use of thyroid extract.

Swan[26] reports a very interesting case of myxedema in which auricular fibrillation appeared when thyroid substance was given, ceased when thyroid was discontinued, but reappeared when the drug was readministered. Again the therapy was stopped and the rhythm became regular. In his case the electrocardiogram showed a prolongation of the P-R interval (0.24 seconds).

CARDIAC PATHOLOGY IN MYXEDEMA

Little is known concerning the pathological findings in the heart in myxedema. After extirpation of the thyroid gland, Kish[27] and Bensen[28] have found degenerative changes in the myocardium, describing first the loss of transverse striations with granular disintegration; and, later, cloudiness of the muscle fibers. C. Wegelin[29] in an exhaustive study of the thyroid states that the most common anatomical finding was the dilatation of the heart.

Goldberg[30] performed thyroidectomies in sheep and goats. In 11 out of 17 sheep he found calcification of the aorta, cardiac dilatation and a degree of atherosclerosis not found in his control animals. He described a flabby myocardium in which microscopically no cross striations could be seen. The fibers were found to be densely packed with deeply staining nuclei. There was also vacuolation of the Purkinje fibers. A common post-mortem finding was calcified placques in the pulmonary artery and in the thoracic and abdominal aorta.

Schultz[31] found a peculiar infiltration of mucoid substance and a thickening of the aortic valves. He also found a disintegration of the muscle fibers.

Other observers have noted the sclerotic processes in the aorta and coronary arteries. A. Fishberg[32] pointed out the frequency of atherosclerotic changes in myxedematous patients involving commonly the kidneys, and frequently associated with hypertension and myocardial insufficiency. In discussing the myxedema heart, he suggests that arteriosclerotic changes may indirectly play a rôle in the pathogenesis of this condition. These observations have been frequently made in myxedema. It will be recalled that in Meissner's second case (see above) there was an associated hypertension and chronic nephritis. These findings may well explain the failure in the reduction of the cardiac volume after thyroid administration in some cases.

In an experimental study of the morphology of the heart muscle in hypothyroidism, Brooks and Larkin[33] performed thyroidectomies on rabbits, the animals being examined after death, which varied from two to forty-three days postoperatively. These authors conclude that

cardiac signs of myxedema are not due to alterations in the myocardium because no characteristic pathological picture could be detected in their studies.

MECHANISM OF THESE CHANGES

The last authors quoted emphasized the observations that the cardiac signs in myxedema appear quite early. They do not believe that these changes are of an anatomical character, the relief following thyroid treatment being against this theory. Means and his collaborators consider the cardiac changes to be functional, directly due to thyroid insufficiency as proved by the relatively rapid response to thyroid therapy. They differentiate this type of case from those myxedematous hearts in which there are organic changes.

Zondek, in his first paper, raised the question regarding the mechanism in the cardiac reduction in this disease. He states that there is dilatation of the heart and not hypertrophy. He reasons as follows:[34] the heart becomes smaller with an increased stimulation of the accelerator nerve or with an inhibition of the vagus nerve. This can be recognized by an increase in the pulse rate. In his cases, there was an increase of 20 beats per minute, which in itself does not explain the decrease in the size of the heart. Hence, he concludes that thyroid substance acts on the heart muscle itself. He draws an analogy with Kramer's studies of the skeletal muscle in myxedema in which he finds an inhibition. By increasing the tonus there is a decrease in the size of the muscle. In his book, *Die Krankheiten der Endokrinen Drüsen*,[20] Zondek attempts to explain the dilatation of the heart and its reduction by two factors: a nervous and a physicochemical one. He points out that the sympathetic is the tonus nerve to the myocardium and that myxedema is characterized by a high grade of sympathetic irritability, which is seen in the hypotonus of the myocardium which in itself may lead to a chronic dilatation. Thus it leads to serious myocardial injuries, the muscle fibers and connective tissue being filled with an edematous fluid, quite like the mucoid connective tissue of the skin in myxedema. The thyroid stimulates the sympathetic, and the cardiac tissues become markedly dehydrated.

Zandren[35] noted the disproportion between the objective cardiac findings and the severe subjective symptoms of insufficiency in certain cases of myxedema heart. In his paper, he discussed Eppinger's theories of edema at length and suggests that the cases described as myodegeneratio-cordis by Eppinger may belong to the same class as the cases of myxedema heart described by Zondek. The results of thyroid therapy accomplished by both authors suggested this to Zandren. He thus explained the mechanism of the thyroid in Eppinger's cases.

SUMMARY

1. Myxedema heart is characterized by an enlargement of all four chambers, slow pulse rate, a normal blood pressure, and electrocardiographic changes.

2. The myxedema heart was first described in 1918 by Zondek, who observed the cardiac hypertrophy and demonstrated the reduction in size after giving thyroid substance.

3. Not all cases reported in the literature are typical examples of myxedema heart. Many authors omit electrocardiographic and x-ray studies. It is possible that certain patients were suffering from coronary artery disease.

4. A case is reported of a fifty-eight-year-old man who presented the typical signs and symptoms of thyroid insufficiency. In this case the teleroentgenogram showed an enlargement of the right and left ventricles. The basal metabolism rate was minus 20 per cent. The electrocardiogram revealed a low voltage in all three leads, a left ventricular preponderance, and a notching and prolongation of the QRS complexes in all leads. After treatment with thyroid substance there was clinical improvement in the myxedema, but no demonstrable changes were observed either in the x-ray outline of the heart or in the electrocardiograms. The second case reported was that of a young man of twenty-six years, whose basal metabolism rate was minus 18 per cent. The electrocardiogram was not characteristic in this case.

5. Many electrocardiographic studies have been made in hypothyroidism. Absent P- and T-waves are well known. Widening and notching of the QRS complexes, and negative T-waves have been described. Low voltages are known to occur. All these characteristics usually disappear after thyroid medication.

6. Theories which explain the above changes are discussed.

7. Methods of safe administration of thyroid gland products and dosage are recorded.

8. There are probably two groups of cases of myxedema heart: those which respond to thyroid therapy, and those in which a long standing myxedema and other factors produce permanent changes in the myocardium which do not permit of a response to thyroid medication.

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Joseph Sailer

IN THE recent untimely death of Joseph Sailer the medical profession has lost a distinguished representative, and preventive medicine, as it relates to heart diseases, one of its staunchest supporters and most active protagonists.

He was among the first to recognize the importance of the public health aspects of heart diseases and early gave his earnest support to the efforts being made to arouse more general interest in measures for the better control of these diseases. It was due chiefly to his enthusiasm and initiative that the Philadelphia Heart Association was organized and became so potent an agent in advancing the welfare of the heart patient. Later he played a leading part also in the organization of the Pennsylvania State Heart Association and was tireless in his efforts to raise throughout that state the standards of the care of cardiac patients. He was one of the founders of the American Heart Association, was an active member of its Executive Committee until a short time before his death and served as its president from 1926 to 1928.

But his interest in the welfare of sufferers from heart disease, intense as it was, represented only a small part of his activities. For many

years as Physician to both the Presbyterian and the Philadelphia General Hospitals and as Professor of Clinical Medicine in the Medical School of the University of Pennsylvania he won fame as a wise clinician and a successful teacher. Upon every phase of his professional work he brought to bear keen insight, sound judgment and a scientifically trained mind.

The world is poorer for the passing of Joseph Sailer and those of us who were privileged to be counted among his many friends have lost a loyal and warm-hearted comrade.

Department of Reviews and Abstracts

Selected Abstracts

Palmer, Robert S., and White, Paul D.: A Note on the Continuous Humming Murmur Heard in the Supra and Infraclavicular Fossae and Over the Manubrium Sterni in Children. New England J. Med. 199: 1297, 1928.

Fourteen cases showing the continuous humming murmur best heard on the right side of the neck also heard in the infraclavicular fossae over the manubrium sterni and sometimes on the left side of the neck, have been reviewed in order to call attention to a common physical sign in childhood. In this series of fourteen cases, patent ductus arteriosus was wrongly considered three times and aortic regurgitation was wrongly considered twice.

When the chin is raised and turned to the left this murmur will often be heard in children when otherwise it is not present. It may be heard by this maneuver in some adults.

Although most writers hold that the murmur arises in the veins, this theory is not yet proved. The fact that it is like the murmur of patent ductus arteriosus, the observation that it does, in some cases, persist in spite of occluding the vein, and its great variability in intensity with respiration require further study and observation to determine the exact mechanism of the production. It is possible, as Laennec first thought, that the murmur may arise in the arteries. At any rate the air spaces probably play an important rôle, whatever the vascular origin.

Lawson, George M., and Palmer, Robert S.: Occurrence of Subacute Bacterial Endocarditis in Childhood. New England J. Med. 199: 1205, 1928.

At the Massachusetts General Hospital, the earliest age at which subacute bacterial endocarditis has occurred is six years and the next earliest is eight years, a third case is age ten years.

A very unusual case of Streptococcus viridans septicemia without evidence of valvular damage in a child twenty-one months is reported. The appearance of the colonies cultured from the blood of this case suggests that it belongs to the subacute bacterial group.

Irvine-Jones, Edith, I. M.: Skin Sensitivity of Rheumatic Subjects to Streptococcus Filtrates. Arch. Int. Med. 42: 784, 1928.

The author based her study on a varied group of streptococci obtained from the upper respiratory tract of rheumatic subjects and contrasted the findings with the culture group from nonrheumatic individuals. The organisms were classed according to their reactions on blood agar, according to their fermentation tests and according to the skin reactions obtained when filtrates of the strains were injected intradermally into rheumatic and nonrheumatic subjects. Correlation with the Dick test enabled the strains to be differentiated from scarlatinal forms of streptococci.

It was found that the series of organisms from rheumatic sources were very similar culturally and immunologically to those from normal individuals but

that skin sensitivity to filtrates from either series of strains was very much more marked in rheumatic individuals than in the control subjects. This increased sensitivity of rheumatic subjects was more clearly demonstrated with the anhemolytic than with the hemolytic forms.

The skin sensitivity was most marked in subjects during the acute phases of rheumatism, negative reactions frequently occurring as convalescence was established.

The author followed certain rheumatic subjects for a considerable period of time and was able to correlate the changes in the intradermal injection with the clinical condition of the subject and analogy could thus be drawn between her findings and those of Dochez and Stevens on experimental allergy.

The author concludes that rheumatic fever is an allergic manifestation due to streptococci occurring in predisposed individuals. The evidence would point to a heterogeneous group rather than one particular strain of streptococcus *as being responsible* for rheumatic fever.

Clawson, B. J.: Experimental Rheumatic Arteritis. Arch. Path. 6: 947, 1928.

In this paper a description is given of certain arterial lesions that were produced experimentally. Streptococci had been repeatedly injected into monkeys in an effort to produce glomerulonephritis. Microscopic examination showed in the kidneys of two of the monkeys vascular changes which bore a resemblance to the lesions described by Klotz and Pappenheimer and von Glahn. The two monkeys had received intravenous injections of strains of Streptococcus viridans, isolated from the blood of patients having acute rheumatic fever.

In another series of experiments in which many rabbits had had streptococci injected intravenously or subcutaneously in the effort to produce, experimentally, Aschoff bodies and subcutaneous rheumatic nodules, similar examples of arteritis were noted. This arteritis was commonly found in the hearts of rabbits into which streptococci had been injected intravenously, and practically always in the subcutaneous tissues of rabbits into which the streptococci had been injected subcutaneously.

The result of these experiments showed that by injecting streptococci into rabbits and monkeys lesions could commonly be produced in man which morphologically appeared similar to the rheumatic lesions in many. The morphology of the cellular reaction in this experimental arteritis was similar to that found in the Aschoff nodule and in rheumatic inflammation in other parts of the body.

Clawson, B. J.: Experimental Subcutaneous Rheumatic Nodules. Am. J. Path. 6: 565, 1928.

In this paper a microscopic study is made of human subcutaneous rheumatic nodules and of the nodules produced experimentally in the subcutaneous tissue in rabbits by injecting streptococci. The purpose is to compare the structure of a known rheumatic lesion with that of a lesion which has been produced experimentally to arrive at further conclusions concerning the casual relation of streptococci to rheumatic injections.

The nodules were produced in the subcutaneous tissues of rabbits by injecting different strains of streptococci in varying amounts and at different intervals under varying conditions. Five different strains of streptococcus were used. Two of these were isolated from the blood of patients having acute rheumatic fever, one from the blood of a patient with subacute bacterial endocarditis and two from pus from sinuses in cases of sinusitis.

Ten rabbits were injected intracutaneously and subcutaneously in many places with these organisms. Most of the animals had been previously injected

with strains of streptococci intra-arterially through the left ventricle of the heart. Others had been previously injected subcutaneously in one area with a mixture of streptococci and agar.

The reaction found in the injected areas depended on the virulence of the organism, the number of organisms injected and the time of the removal of the nodules after injection. The most virulent organisms tended to produce local abscesses, also if the area of injection was excised shortly after injection, there were signs of abscess formation. If organisms of low virulence were used or if small numbers of organisms were injected if the area of injection was excised at a later day there were found typical proliferative nodules at the site of injection. The reaction observed in these nodules was similar to those found in the nodules removed from human beings. Since these experimental nodules occur obviously as a result of injected streptococci, the probable conclusion is suggested that acute rheumatic fever and the type of inflammation associated with it are of streptococcic origin.

Kreidler, William A.: Biologic and Serologic Studies of Streptococcus Cardio-arthritidis. J. Infect. Dis. 43: 415, 1928.

The author has studied the biologic and serologic reactions of a series of 107 strains of this organism. Three strains were obtained from blood cultures, three from cultures of feces *and* the remainder from throat cultures. All the strains fermented glucose, sucrose, inulin, salicin and raffinose; none, mannitol. Twenty-one strains failed to ferment *lactose* and failed to produce acid in milk. None liquefied gelatin or produced indol.

Antigens prepared from each of the strains were agglutinated by a monovalent antiserum of S. cardioarthritidis in dilutions high enough to indicate that these strains fall into a definite serologic group and that group agglutinins play but a small part in the results obtained.

When the foregoing facts are considered, there seems to be reason for the belief that these microorganisms biologically and serologically form a compact species of streptococci. The failure of some of the strains to ferment lactose and the difference in the agglutinability of the strains, suggest that there may exist, within the species, immunologic subtypes of this organism.

Belk, William P., and Fendrick, Edward: The Lesions in Animals Inoculated with Streptococcus Cardio-Arthritidis. Arch. Path. 6: 812, 1928.

This report is based on the anatomic lesions found in seven rabbits and two horses inoculated with repeated injections of Streptococcus cardio-arthritidis. The animals were given viable twenty-four hour cultures suspended in saline solution. The lesions in the various tissues of the body resembling those seen in human rheumatic fever were identified. These lesions are described in the paper.

Epicarditis appeared in two of the rabbits; nonpurulent focal myocarditis in six; mural endocarditis in three; valvular endocarditis in four; arteritis in four; myositis in three; bursitis in one; glomerular nephritis in one; infarcts of spleen and kidney in one; aortitis in three and pneumonitis in all the animals. Pericarditis, focal myocarditis, valvular endocarditis, arteritis and pneumonitis appeared in both horses.

Poynton, F. John: Rheumatic Heart Disease in Childhood. Lancet 215: 537, Sept. 15, 1928.

In these 3 lectures, the author discusses three particular phases of rheumatic heart disease. First, the correlation of the pathological lesions of the heart

with other rheumatic lesions; second, the clinical manifestations of rheumatic heart disease and third the treatment of heart disease.

The author describes the two chief ways in which acute rheumatism damages the heart and other organs, assuming that a streptococcus is the cause of the disease. In the first process there are the local interstitial lesions which tend to necrosis and fibrosis and in the second process there are the toxic effects of the circulating poisons. The interstitial lesions produce results which clinical observation at the bedside corroborates: valvular lesions, pericarditis and local myocardial disturbances. The toxic effects of the infection though well recognized at the bedside in the profound anemia and damage to the cardiac muscle and nervous system cannot yet be correlated with any definite poison. The author regards chorea as a rheumatic meningo encephalitis.

Campbell, John S.: Stereoscopic Radiography of the Coronary Circulation. Lancet 215: 168, July 28, 1928.

The author has devised a method of infusing human hearts for roentgen examination. A preparation of barium, Rontyum has been found to give the best results. This is injected in the vessels of the heart under a pressure of 280 mm. of mercury maintained for three minutes. After injection of both coronary arteries, the chambers of the heart are packed with wool and the organ immersed in 10 per cent formalin for twenty-four hours to secure fixation in the best position for stereoscopic examination. This simple method has been found to give satisfactory pictures.

The skiagrams demonstrate very clearly the finer ramifications of the cardiac vessels while small variations in their caliber can be readily noted. The variations in the distribution of the coronary vessels noted by Gross have been confirmed but their occurrence has been greater in this present series of 92 hearts examined by the author.

The alteration in the relative vascularity of the ventricles which comes with advancing age and results in a decrease of the blood supply to the right heart through an increase in the development of anastomotic branches was also verified. Diminishing vascularity of the heart similar to that found in senility was found to accompany coronary disease.

Removal of portions of the ventricular walls made possible a stereoscopic study of the septal circulation and the supply of the neuromuscular tissues.

Whitten, Merritt B.: A Review of the Technical Methods of Demonstrating the Circulation of the Heart. A Modification of the Celluloid and Corrosion Technic. Arch. Int. Med. 42: 846, 1928.

The author reviews the literature pertaining to methods used in preparing casts of the interior of the heart and of the coronary circulation. He also described his own technic for preparing specimens using celluloid as the material for forming a cast and the corrosion method for destroying the heart tissues. The left coronary arteries in the completed specimen are injected in red, the right coronary arteries in blue and the coronary veins in white. The wall of the heart is destroyed and the background of the vessels is the white cast of the chambers of the heart, depicting the internal surface of the heart area.

Dumas, A.: Hypertensive Form of Mitral Endocarditis. Presse Med. Sept. 15, 1928.

The author finds that 9 out of 40 cases of chronic endocarditis which were confirmed by autopsy were accompanied by hypertension. He notes that this association is commonest in subjects over 50. The mode of death in 6 of the 9

instances was by progressive weakness and failing tension. In 3 of the cases death occurred more rapidly with edema of the lungs and in these cases the heart showed very little hypertrophy.

The clinical findings in such cases are of pure hypertension. No nephritis was present and a few old infarcts were found which could be due to the heart condition. Little cardiac hypertrophy was present and albuminuria was only an occasional finding.

The etiology of the mitral disease is doubtful. In two cases, acute articular, rheumatism had been noted in the history and in one instance syphilitic aortitis was present.

The physical signs of the heart are generally those of mitral insufficiency although autopsy shows definite stenosis.

In some cases a presystolic murmur was heard and was confused with the gallop rhythm of a hypertensive heart. In some subjects the lesion is silent.

The author considers the mitral endocarditis as responsible for the development of the mitral stenosis.

Herrick, James B.: Treatment of Heart Disease. J. A. M. A. 91: 1761, 1928.

In this address the author apologizes for a very simple, old-fashioned paper. He points out that plain truths have to be repeated or presented in forms to fit the passing moment. He discusses the all-important subject of rest and digitalis, pointing out the difficulties in determining in each individual patient just what degree and kind of rest and medication are necessary. He believes there is no hard and fast rule for these two phases of treatment.

Hepburn, J., and Graham, Duncan: An Electrocardiographic Study on 123 Cases of Diabetes Mellitus: Am. J. M. Sc. **176:** 782, 1928.

It has been shown that in a series of 123 diabetic patients 56 showed serious electrocardiographic abnormalities at the beginning of the diabetic treatment and that in a very fair percentage the electrocardiogram returned to normal after the diabetic condition was controlled by treatment. It would appear from these observations that in the cases in which the electrocardiograms returned to normal after the diabetic condition had been controlled, that the abnormal electrocardiograms had resulted from the effect on the myocardium of the perverted metabolism present in diabetes mellitus. The authors discuss whether these changes might be due to a direct action on the myocardium or an indirect one resulting from disease of the coronary artery. None of the few cases of severe acidosis studied showed an abnormal electrocardiogram and many severe diabetics with hyperglycemia had normal electrocardiograms. They conclude that diabetes mellitus apparently does not produce any direct effect on the myocardium resulting in an abnormal electrocardiogram. The changes in the electrocardiogram found in this study resembled those seen in nondiabetic patients suffering from cardiovascular disease and are supposed to result from the indirect effect produced on the myocardium from disease of the coronary artery.

Lemann, I. I.: Coronary Occlusion in Buerger's Disease (Thromboangiitis Obliterans): Am. J. M. Sc. **176:** 807, 1928.

In thromboangiitis obliterans the pathological process is probably not limited to the vessels of the extremities. Affection of the coronary vessels has been reported in three cases collected in the literature. The author reports another case showing extreme arteriosclerosis. The lesion of thromboangiitis obliterans was not present in the coronary artery.

Bromfin, I. D., and Simon, Saling: Observations on Some Cardiac Lesions Coincident With Pulmonary Tuberculosis. Am. Rev. Tuberc. 18: 727, 1928.

The incidence of valvular heart disease in pulmonary tuberculosis recognizable clinically is only about 6 per cent in the experience of the authors. Dyspnea out of proportion to the pulmonary involvement especially when there are no constitutional symptoms should arouse the suspicion of an existing cardiac affection.

Artificial pneumothorax when indicated in such cases should be administered with great caution. The earliest manifestation of cardiac disturbance is an indication for discontinuing the pulmonary compression.

Complete bed rest must be rigidly enforced for a longer period of time than in cases not complicated by heart disease.

The electrocardiogram is often of value in determining the cause of obscure cardiac symptoms. The authors found an instance of bundle-branch block in a patient without symptoms indicating such a disturbance of mechanism.

Starr, Isaac Jr., and Gamble, C. J.: An Improved Method of Determination of Cardiac Output in Man by Means of Ethyl Iodide. Am. J. Physiol. 87: No. 2 450, 1928.

The authors have modified the ethyl iodide method of Henderson and Haggard for the estimation of the cardiac output. In their earlier papers they showed that the coefficient of distribution of ethyl iodide between air and blood as originally expressed by Henderson and Haggard could not be confirmed, neither was the ethyl iodide destroyed in one round of the circulation as was originally thought.

By continuing a modification of this method with the Fick principle, the authors have obtained reliable results in men.

Several technical points stressed by the authors include:

1. The estimation of the ethyl iodide in air by the precipitation of silver iodide in the distillation of the blood previous to determination. The authors use capryl alcohol to reduce the pressure.

2. The amount of blood used has been raised to 60 c.c., thus permitting a reduction in the concentration of the ethyl iodide used.

3. The distribution coefficients of the blood previously reported by the authors to average 7.6 is, they believe, lower as with bigger samples it averaged 6.1. The presence of fever or of anemia lowered this figure and the figure for dogs is higher, averaging 10.7.

The authors demonstrated in dogs and in human subjects that the arterial ethyl iodide may be estimated from that of the alveolar air and that the ethyl iodide content of mixed venous blood may be estimated from the rebreathed air.

They were able to get consistent fugures for blood flow in dogs by the ethyl iodide method when the lungs were perfused at a known rate.

A description of various manifestations of the apparatus is given with consecutive determination on two subjects. The method requiring no active cooperation from the subjects employed.

Eppinger, H., Lazlo, D., and Schürmeiyer, A.: On the Probable Causes of Waste of Energy in the Organism with Heart Failure. Klin. Wchnschr. Jahrg. 7, No. 48, 2231, 1928.

The authors have correlated the problems of hemodynamics with those of metabolism. Patients with cardiac decompensation use more oxygen in relation to their size than normal individuals and it is found that after exercise an

excess of lactic acid is present in their blood. This latter points to faulty muscle metabolism during work with failure of reconversion into glycogen. That this is evidently not entirely due to a deficient supply of oxygen is shown by the fact that the arterial oxygen is generally normal in amount. It is suggested that the explanation may be similar to that described by Eppinger as occurring in shock and collapse; namely, an altered distribution of the blood between circulation and tissues, so that the arterial blood volume and hence the supply to the muscles is decreased.

In histamines and more especially in peptone shock and failure in blood pressure occurred and the fatigue curve of the muscle corresponded to this; as the blood pressure rose the fatigue picture disappeared.

To show the effect of local change in circulation the authors ligated the femoral artery and vein ten minutes. Only minor changes in the muscle were observed while ligation of the aorta lead to changes resembling those of shock. Ligation of the vena cordis did not produce any marked change. Bleeding and suffocation produced rapid fatigue, but no change unless the oxygen was reduced below 8 to 10 per cent.

The lactic acid of muscle and blood under the above-mentioned conditions was studied and it was found that during histamine and peptone shock and after ligation of the aorta that the lactic acid was increased in the muscle. Decrease of oxygen in the air did not alter the lactic acid as long as the minute volume could be increased.

The authors consider that the failure of resynthesis of lactic acid into glycogen as due to circulatory insufficiency with oxygen lack in the muscle.

In narcotized dogs studied from the standpoint of shock and ligation of the aorta with and without work there was an increase in the oxygen consumption due to a diminished resynthesis of lactic acid into glycogen.

To demonstrate the effect of shock on the blood supply to the muscles, the author observed a cat muscle under the microscope using Krogh's technic. Histamine produced a stasis in arteries and veins and agglutination of the red blood corpuscles. The effect of muscular work on the minute volume in histamine shock was also observed and a decrease noted. The volume of circulating blood was not estimated but it is assumed from previous observations that in decompensation considerable amounts of blood are deposited.

Thus the authors believe that capillary damage leading to deposition of blood and diminution of the blood volume occurs in decomposition. This results in a diminished oxygen supply in the tissues, so that lactic acid is not reconverted into glycogen.

Eppinger, H., and Hinsberg, K.: On the Possibility of a Peripheral Treatment of Patients with Heart Disease. Klin. Wchnschr. Jahrg. 7, No. 48, 2284, 1928.

From the foregoing paper, the authors draw certain conclusions for the treatment of heart disease and suggest massage as well as the usual drug therapy. They show in three patients with chronic heart disease that a general massage of the muscles leads to a reduction of the oxygen debt and the oxygen consumption during work. Besides the objective findings, the subjective conditions of the patients were improved. They recommend the use of massage in patients with chronic heart failure after the stage of decompensation.

Eyster, J. A. E.: Experimental and Clinical Studies in Cardiac Hypertrophy. J. A. M. A. 91: 1881, 1928.

The increase in the muscle mass of the diseased heart occurs mainly in that part of the heart placed under a mechanical handicap as a result of a

lesion. The theory of work hypertrophy has been almost universally accepted in explaining this increase in size as a result of the increased activity and work necessary to overload the mechanical defect.

It has been pointed out by Albrecht that in human hearts the seat of myocardial disease, the stimulus to hypertrophy may be impaired nutrition resulting in work hypertrophy. The author has pointed out previously that dilatation of the heart muscle precedes hypertrophy in cardiac lesions and in several types of experimental lesions produced in dogs he has shown by roentgenologic methods that a period of increase in heart volume occurred immediately after the lesion was produced associated with macroscopic and microscopic evidence of stretching and injury to the muscle. This initial increase in volume disappeared after a few days and the heart returned to its normal volume or even below. Subsequent to this transitory period of stretching and dilatation, a second and more gradually developing increase in heart volume occurs which is due to increase in muscle mass or hypertrophy. This is completed as the result of a single lesion in approximately one hundred days. A second lesion, superimposed on the first causes a second period of transitory dilatation and the subsequent period of additional hypertrophy.

As a result of these studies, the author proposes a new theory as to the cause of heart muscle hypertrophy. This theory in contrast with the theory of work hypertrophy may be designated as the theory of injury hypertrophy and he ascribes increase in muscle mass not to a physiological response to increased work but to a tissue response of some nature to actual injury. During the period of stretching the muscle fibers are the seat of a process of hydropic degeneration, a typical injury and reaction to injury.

In order to test this matter further temporary cardiac overload was produced in a series of dogs by massive transfusions. The estimated blood volume was increased from 75 to 100 per cent in a series of 11 animals. These have shown an initial dilatation comparable with in every way to that produced by aortic lesions, except that it lasts for a somewhat shorter period. During this period the ventricular muscle shows similar macroscopic evidence of stretching and injury. The heart volume then returns to near its normal or even below as also occurs after aortic lesions, and finally shows a second more gradually developing increase in volume due to hypertrophy of the muscle. A second massive transfusion leads to a repetition of the whole process, a second period of dilatation being succeeded by a second period of additional hypertrophy, comparable again to the production of a second experimental lesion superimposed on the first.

Estimating the heart size by the use of x-rays and certain other methods of physical examination, the author has studied 70 men and 40 women forming a group of university athletes. The author believes that in abscence of cardiovascular disease that cardiac hypertrophy in man does not exist.

He concludes from these experimental and clinical observations, that the most important factor leading to the cardiac hypertrophy that develops in organic cardiac or vascular disease is not increased work of the muscle per se but the muscle injury and the reaction to injury that results from abnormal stretching of the muscle in the initial period of overload as the lesion develops.

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CARDIAC PAIN

A Consideration of Its Nosology and Clinical Associations*

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PAIN in the region of the heart is a common complaint. Of the last five hundred patients who have come to the consulting room, 15 per cent have described pain referred to the sternum or precordium either as the chief source of discomfort or as one of several complaints. Its significance for the patient may be trivial or grave; but since Heberden's memorable communication, the occurrence of such pain has come to carry with it, in the minds of the laity and indeed, in the judgment of many physicians as well, the sinister suggestion of sudden death.

HISTORICAL

It was on July 21, 1768, that William Heberden, a distinguished London practitioner, read before the Royal College of Physicians a paper entitled *Some Account of a Disorder of the Breast*.[1] Because our knowledge of this condition and also the still unfinished controversies concerning its nosology were initiated by his masterly description, it is desirable to give quotations from the original text.

"There is a disorder of the breast, marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it, and not extremely rare, of which I do not recollect any mention among medical authors. The seat of it, and sense of strangling and anxiety with which it is attended, may make it not improperly be called Angina Pectoris.

"Those, who are afflicted with it, are seized, while they are walking, and more particularly when they walk soon after eating, with a painful and most disagreeable sensation in the breast, which seems as if it would take their life away, if it were to increase or to continue: the moment they stand still, all this uneasiness vanishes. In all other respects, the patients are, at the beginning of this disorder, perfectly well, and in particular have no shortness of breath, from which it is totally different. . . .

*From the Department of Medicine, College of Physicians and Surgeons of Columbia University and the Presbyterian Hospital.
Read before the Rochester Medical Association and Rochester Academy of Medicine, Rochester, N. Y. November 7, 1928.

"When I first took notice of this distemper, and could find no satisfaction from books, I consulted an able physician of long experience, who told me that he had known several ill of it, and that all of them had died suddenly. This observation I have reason to think is generally true of such patients, having known six of those, for whom I had been consulted, die in this manner. . . . But though the natural tendency of this illness be to kill the patients suddenly, yet unless it have a power of preserving a person from all other ails, it will easily be believed, that some of those, who are afflicted with it, may die in a different manner, since this disorder will last, as I have known it more than once, near twenty years, and most usually attacks only those who are above fifty years of age. . . .

"The os sterni is usually pointed to as the seat of this malady, but it seems sometimes as if it was under the lower part of it, and at other times under the middle or upper part, but always inclining more to the left side, and sometimes there is joined with it a pain about the middle of the left arm. What the particular mischief is, which is referred to these different parts of the sternum, it is not easy to guess, and I have had no opportunity of knowing with certainty."

It was the astute Edward Jenner who first threw light on the nature of this "mischief." In 1776, John Hunter had his second heart attack, and was visited at Bath by his pupil, Jenner. To Heberden, Jenner then wrote a letter, giving his diagnosis of Hunter's malady and suggesting, for the first time, the probable association of coronary artery disease and cardiac pain.[2] In a later letter, published by Parry in 1799,[3] Jenner gives a fuller account of his findings and states that he did not publish his views because he feared that they might be a source of worry to his friend, Hunter. This pathological description is also worth quoting.

"The first case I ever saw of Angina Pectoris, was that in the year 1772, published by Dr. Heberden with Mr. Hunter's dissection. There, I can almost positively say, the coronary arteries were not examined. Another case of a Mr. Carter, at Dursley, fell under my care. In that, after having examined the more important parts of the heart, without finding anything by means of which I could account either for his sudden death, or the symptoms preceding it, I was making a transverse section of the heart pretty near its base, when my knife struck against something so hard and gritty, as to notch it. I well remember looking up to the ceiling, which was old and crumbling, conceiving that some plaister had fallen down. But on a further scrutiny the real cause appeared: the coronaries were become bony canals. Then I began a little to suspect. Soon afterwards, Mr. Paytherus met with a case. Previously to our examination of the body, I offered him a wager that we should find the coronary arteries ossified. This, however, proved to be not exactly true; but the coats of the arteries were hard, and a sort of cartilaginous canal was formed within the cavity of each artery, and there attached, so however as to be separable as easily as the finger from a tight glove. At this very time, my friend Mr. John Hunter began to have the symptoms of Angina Pectoris too strongly marked upon him; and this circumstance prevented any publication of my ideas on the subject, as it must have brought on an unpleasant conference between Mr. Hunter and me. I mentioned both to Mr. Cline and Mr. Home, my notions of the matter, ... but they did not seem to think much of them. When, however, Mr. Hunter died, Mr. Home very candidly wrote to me, immediately after the dissection, to tell me I was right."

Whether priority for the description of what Heberden termed "Angina Pectoris," should be given to Seneca (1605), Morgagni (1761) or to the Frenchman, Rougnon (Feb. 1768) is a matter of some historic interest but is not pertinent at this time. How the clinical concept which Heberden portrayed was viewed by those who followed, and in what manner controversial discussion arose, is directly related to the development of present day thought. Only a few of the steps in the argument will be touched upon.

Parry, in 1799,[3] was among the first to sense the difficulty of adhering closely to the criteria laid down by Heberden, and to point out that cases described by other observers as angina pectoris did not conform to one pattern. He believed that the symptoms in one reported case were due to hydropericardium, in another to aneurysm of the aorta and in a third to "suppuration between the two bags of the pleura, where they constitute the mediastinum." In other instances, he questioned the accuracy of the diagnosis, saying that the "cases of MacBride and Smith of Dublin, are evidently cases of palpitation of the heart, such as every physician of extensive practice must have often seen"; another, "was a mere affection of the respiratory organs, a violent spasmodic asthma, . . . which never occurs in the pure Angina Pectoris." Parry then proceeded to add to the confusion by concluding that "the Angina Pectoris is in reality a case of fainting. . . . All the circumstances in the Angina Pectoris preceding the actual Syncope are approaches towards it; and in every uncombined and recent case, like those which I have described, the patient probably dies with no other symptoms than those which shew an irrecoverable diminution of the motion of the heart." Parry's monograph is entitled *An Inquiry into the Symptoms and Causes of the Syncope Anginosa, commonly called Angina Pectoris.* This is the first sign of dissension from Heberden's terminology.

Hope[4] in 1839, heads a chapter in his book *Neuralgia of the Heart, or Angina Pectoris,* in "presenting the train of symptoms which have been denominated by Dr. Heberden *angina pectoris.*" He points out that "different physicians have found it connected with different organic lesions or states, and each has supposed it to be occasioned by that, with which he has most frequently found it co-exist. Dr. Parry, and after him Burns and Kreysig, ascribe it to ossification of the coronary arteries; Dr. Hooper, to affections of the pericardium; Dr. Hosack to plethora; Dr. Darwin, to asthmatic cramp of the diaphragm; Drs. Butler, Macqueen, and many others, have regarded it as a particular species of gout; Dr. Latham has found it connected with enlargements of the abdominal viscera, while the thoracic viscera were sound; and Heberden, having found it both connected and unconnected with organic disease, thinks that its cause has not been traced out, but that it does not seem to originate necessarily in any structural derangement

of the organ affected.'' Hope expressed the opinion that "it may originate in any cause, whether organic or functional, capable of *irritating* the heart, or of rendering it morbidly susceptible of irritation; and as structural disease of the organ has this effect more than other cause, it is that on which the malady, in its severer forms, is most frequently dependent.''

Latham,[5] 1845, flatly refused to accept angina in the sense of Heberden. Says he: "There is one eminent instance in which an assemblage of symptoms is thus made to bear the name of a disease; angina pectoris.'' There follows a description of the variety of pathological states found at necropsy in cases so diagnosticated during life; as well as the statement that "it has existed where no form of disease or disorganization whatever has been found either in the heart or in the blood vessels nearest to it.''

In the experience of the English observers, angina was a rare affection. In contradistinction to the rarity of genuine angina pectoris, Walshe[6] in his textbook, says that he frequently met "with a form of complaint combining in a minor degree many of the characters of angina; and to this imitation of the true disease I propose to give the name of pseudo-angina.'' Walshe found pseudo-angina as an attendant on various diseases: gout, rheumatism, anemia, hysteria, spinal irritation, epilepsy, intercostal and mammary neuralgia. The points of differential diagnosis between genuine and pseudo-angina are but briefly mentioned. Yet this author is apparently the first to express the idea that cardiac pain may occur in many conditions in which the heart is not primarily the seat of the trouble.

Like Hope, Laennec[7] classifies angina pectoris as a neuralgia of the heart. Though familiar with the necrospy findings of the English authors and having found various diseased states of the heart and aorta in patients with this complaint, he was particularly impressed by those cases showing no demonstrable lesions on post-mortem examination. He was inclined to ascribe the painful sensations to an affection of the cardiac nerves, vagus or sympathetic, analogous to neuralgias elsewhere in the body. Other nerves, cervical and thoracic, he believed, might likewise be involved, either "sympathetically'' or through anastomatic communications with those primarily concerned.

In his monograph on *Angina Pectoris and Allied States,* Osler[8] reiterates Latham's sentiments in saying: "Angina pectoris is not a disease, but a syndrome or symptom group (without etiological or anatomical foundation) associated with complex conditions, organic or functional, of the heart and aorta. Pain about the heart of an agonizing character, occurring in paroxysms, is the dominant feature of all varieties of the syndrome. Used to define paroxysmal attacks of pain in the chest—breast-pang—we employ the term generically, qualifying the varieties by such names as true, false, hysterical and vasomotor.''

But such generic use of the term has not served to clarify the picture. The distinctions between syndrome and disease are not apparent in this definition.

Among those who gave much scholarly thought to this subject was the late Sir T. Clifford Allbutt, as evidenced by his two volumes on *Diseases of the Arteries, including Angina Pectoris.* Several years ago, having published a short paper on cardiac pain,[9] I ventured to write to Cambridge to Sir Clifford asking for his comment. On October 7, 1924, not long before his death, he answered in a letter, expressing what were perhaps his last ideas on this subject. I am taking this opportunity to make them public.

"The difficulty of defining angina pectoris is great because it has so many simulations, and it is hard to exclude these; e.g., tobacco angina, neurotic, and (I think) a tiresome wedge of wind in the lower esophagus which oppresses certain persons painfully on walking—though they can climb hills and stairs, etc., without any—or any more distress and it does not *stop* the patient; he *can* go on, although oppressed. This is commoner in women? I was far from opposing your point of view, one I have urged myself in many contexts. I would have such words as 'asthma' kept strictly to their own (or one) meaning (not 'cardiac' asthma, etc.). So I think *angina pectoris* should be pinned down to substernal (or epigastric) pain, (very rarely in the 'precordial' area) apt to shoot in certain definite directions, and having nearly always a sinister touch about it. It *stops* a man to vague apprehension. This of course is no 'definition'; but what disease *can you define?* It can only be a *description;* longer or shorter. You cannot *define* even a cat. And please do not put 'morbid entity' upon me; it is one of the last remnants of medical ontology—a relic of terminology. But an angina pectoris due to syphilitic aortitis *only* there is, and frequently. Comparatively young persons *don't die* of angina—indeed *directly no one* does: he dies of heart shock—vagus- or ventricular fibrillation due to the afferent pain. The young, sound heart does not *die of it,* horribly as the patient may suffer. We all agree about the spinal segments concerned and referred pains from the pathologic seat of the pain. Not Mackenzie only but also Head and others have worked these out long ago. Mackenzie contends the pain *originates* in the cardiac muscle; but no *afferent nerve* enters muscle—the heart when touched or pricked is insensitive. The pain arises in the *investments* which are *full of* sensory end-organs—the pain is due to a drag upon these—pericardial rarely, aortic in the large majority. Pain in skeletal muscles arises in the investments and fibrous scaffold—the heart muscle has no such fibrous strands. You will see in my book I do not attribute *all* cases of angina pectoris to the periaortic tissue—a few I describe as pericardial. Coronary artery disease is concerned only with *death* in angina pectoris; not with the seat of its origin. 'Hypertension' does not cause angina pectoris if the aorta is sound; it sometimes does arouse it in an aorta not quite sound, but which would not have resented moderate pressure. Aneurysm is merely a cause of aortic disease. Thrombosis may cause exquisite pain if sudden—e.g. embolic, because it puts the arterial investment to sudden strain. In a word, angina pectoris is *not* 'cardiac' pain except in so far as you include in some few cases its outer coat. Neuroses *are not* angina pectoris at all; they are generally intercostal neuralgias. The common submammary ache of cardiacs and menorrhagias, etc., is not angina pectoris. I agree the *clinical* distinctions ought not often to deceive—but a few are hard to read on *one single consultation.* Fasten angina pectoris down to the real thing and you get as much 'definition' as in biology we ever can."

On a small slip of paper, enclosed in the envelope with the body of the letter, was the following: "Angina pectoris is a pain, sometimes slight, sometimes agonizing, arising usually under the sternum and referred in certain definite directions, due to stretching of the outer coat of a morbid aorta; or in a few cases of that of the heart itself. This is my first hasty suggestion for your 'definition.'"

THE MECHANISM OF HEART PAIN

How a painful sensation is produced in the heart is not clear. The myocardium is insensitive to stimuli which are ordinarily productive of discomfort in the periphery of the body. Afferent nerve endings have been found in the outer coat of the blood vessels and in the pericardium. Recent ingenious experiments on dogs[10] have demonstrated that compression of the coronary vessels and immediately adjacent tissue always causes evidences of pain and sometimes produces salivation, vomiting, and changes in the electrocardiogram.

Some sixty-three hypotheses concerning the cause of the symptoms in angina pectoris were collected and tabulated by Huchard.[11] Three theories of pain production in the heart seem worthy of consideration. Allbutt[12] regarded pain in the region of the heart as due to a lesion in the supracardiac aorta, which he termed the "anginiferons area." The lesion, in his opinion, causes "angina" when it penetrates to the outer fibrous investment of the vessel, tension being the factor causing irritation of the nerve terminals. By Mackenzie,[13] the importance of exhaustion of the myocardium was stressed. His hypothesis was summed up in stating that, "while we can reason that pain is the result of exhaustion when the blood supply to the muscle is deficient, we can also conclude that pain results when exhaustion is produced from any other cause, such as great exertion by a healthy heart, or by relatively slight exertion where the muscle is diseased." It was Allan Burns,[14] as Osler has pointed out, who, over a century ago, ascribed the symptoms to anemia of the heart muscle. "Such a state of the arteries of the heart," says he, referring to atheroma, "must impair the function of that organ." In a careful review of the evidence, Keefer and Resnik[15] recently have reached the same conclusion: "the angina pectoris of Heberden has but one cause, anoxemia of the myocardium." This point of view, though at present lacking proof, suggests cogent arguments in its favor. It does not explain all cases. Perhaps more than one mechanism may be concerned in varying circumstances.

THE CLINICAL ASSOCIATIONS OF CARDIAC PAIN

It is evident from the fragmentary account which has been given of the development of thought concerning Heberden's angina, that confusion exists concerning its precise definition. Is every case of paroxysmal breast pain to be so diagnosticated? If not, what are the cri-

teria for this condition? If one of these criteria be sudden death, is it only after the patient's demise that the diagnosis may be made with certainty? For many years, a variable pathological basis has been recognized. The discussion as to the distinctions between "symptom group" or syndrome, and disease has been carried on to no practical purpose. A descriptive term meaning literally, "strangling in the chest," has been perpetuated in spite of protest and acknowledged dissatisfaction. A serious nosologic consideration of the matter is not merely "factitious hair splitting," as Sir Clifford Allbutt would have us believe. Looseness in classification makes for careless thinking; and careless thinking leads to inaccuracies in all forms of scientific procedure.[16]

The pain may vary in its severity, its distribution, and in its relation to exertion. The degree of effort necessary to induce it depends, in a measure, on the individual's sensitiveness to unpleasant stimuli. It is customary to describe as part of the clinical picture of angina a sense of impending dissolution experienced by the patient—the *angor animi* of the older writers. Whether or not this feeling of the nearness of death is present depends largely on the nervous constitution of the sufferer. The work of Gross,[17] and of Oberhelman and Le Count[18] has demonstrated that the coronary arteries, in different subjects, show considerable variation in their origin, distribution, and anastomoses. It follows that the heart as a whole must present functional differences corresponding to these variations when the coronary vessels are diseased—an observation which may account, in part, for the multiplicity of clinical pictures under these circumstances. The rôle of the Thebesian veins in contributing toward an adequate blood supply for the heart muscle must also be taken into account.[19] In the event of gradual closure of the orifices of the coronary arteries, the Thebesian vessels, if allowed time to adapt themselves, can supply the myocardium with sufficient blood to enable it to maintain an efficient circulation. Many factors operate in the determination of the symptoms and signs in a given case.

Those desirous of retaining the term angina, stoutly maintain that it denotes a sharply defined clinical picture, distinguishable from its imitators. So, in contradistinction to true, primary, or major angina, they have described false or pseudo-angina, secondary angina, minor angina, the mock anginas, hysterical angina, angina vasomotoria, tobacco angina and finally, angina sine dolore. Truly, an imposing array of impostors! Differential diagnosis in many medical conditions may be difficult; yet we do not speak of "false appendicitis" because other disturbances in the abdomen may simulate inflammation of the appendix. Our efforts are directed toward describing and correlating symptoms, signs, and anatomical states in order to become familiar with a

train of events which we then call a *disease*. In this concept of disease is implied disorder of both function and structure.

In view of these considerations, and until further knowledge may make a more precise terminology feasible, it is suggested that the use of the term "angina pectoris" be discontinued. In its place, "cardiac pain" may be employed, in each instance qualified by notation of the structural or functional changes with which such pain is found to be associated. A classification formulated on this basis is not, strictly speaking, etiological. But it is workable and encourages more precise diagnosis. Inevitably, better therapy and more accurate prognosis must follow. Such a classification is the following:

Clinical Conditions in Which Cardiac Pain May Be Encountered

I. Affections of the Coronary Arteries.
   1. Stenosis.
      a. Arteriosclerotic.
      b. Syphilitic.
   2. Occlusion.
      a. Arteriosclerotic.
      b. Syphilitic.
      c. Thrombotic.
      d. Embolic (rare).

II. Affections of the Aorta.
   1. Aortitis (with or without Dilatation).
      a. Syphilitic.
      b. Rheumatic.
   2. Arteriosclerosis (with or without Dilatation).
   3. Aneurysm.
      a. Syphilitic.
      b. Arteriosclerotic.
   4. Rupture.

III. Cardiac Valvular Disease.
   1. Aortic Insufficiency.
   2. Mitral Stenosis.
   3. Congenital Heart Disease.

IV. Pericarditis.
   1. Serofibrinous.
   2. Serous.
   3. Adhesive.

V. Poisoning of the Heart by:
   1. Tobacco.
   2. Coffee.
   3. Tea (uncommon)

VI. Disorders of the Hematopoietic System.
   1. Anemia (Primary or Secondary).
   2. Erythremia.

VII. Endocrine Disorders.
1. Thyrotoxicosis.
2. Myxedema.
3. Addison's Disease.

VIII. Cardiac Neurosis (Effort Syndrome).

IX. Pathogenesis Undetermined.

The history and necropsy findings in one unusual case are here given:

A man, aged forty-three years, an electrician, entered the Presbyterian Hospital on December 25, 1924, for the ninth time. In 1918 and again in 1922, he was treated in the ward for influenza. He never had any symptoms of heart disease. His only previous illnesses were typhoid at the age of fourteen and pneumonia at the age of twenty-six. There was no history of syphilis and the Wassermann reaction was negative. In January, 1924, he was admitted with a diagnosis of lobar pneumonia involving the left lower lobe. This was confirmed by x-ray examination. On the second day in hospital, he was suddenly seized with excruciating pain in the precordial area, radiating to both arms. His face was ashen, his lips cyanotic, but there was no dyspnea. The heart sounds became inaudible for a few moments; the blood pressure, twenty-five minutes after the attack, was 70 mm. systolic; 50 mm. diastolic. Morphine and cardiac stimulation brought about comfort and recovery. That evening, a similar, though less severe, attack occurred, relieved by amyl nitrite. An electrocardiogram showed no deviation from the normal. The leucocytes rose from 15,000 to 22,000. A diagnosis of coronary thrombosis was made, although previous examination of the heart and arteries was quite negative. He complained of mild substernal pain on two subsequent occasions and went home on the twelfth day after admission.

Following these episodes the history during the next eleven months was one of progressive cardiac disability. Nocturnal dyspnea appeared and was accompanied by a sense of substernal oppression. Severe attacks of precordial pain were induced on slight effort, making work, even of a light nature, impossible. On six occasions, because of the paroxysms of pain, he was brought to the hospital, sometimes in an ambulance. Many electrocardiograms were taken, some of them showing changes in the T-waves in Leads I and II which were interpreted as indicating active disturbances in the myocardium. Teleroentgenograms showed no cardiac enlargement. There were no signs of valvular disease. As the number of observations increased, the opinion was expressed that coronary disease, with narrowing of the lumen of the vessels, was the pathological lesion responsible for the symptoms. The blood pressure was usually about 124/80 between attacks. Blood counts were normal.

The man was ambitious and eager to work for his wife and six children. The attacks of pain were described as "crushing," "pressing" and "vise-like," precordial or substernal and usually radiating down both arms. Nitrites always afforded immediate relief. At times, nausea and vomiting followed a paroxysm. Cervical sympathectomy was advised with the hope that he might be returned to economic usefulness.

The operation was undertaken on December 26, 1924, by Dr. W. G. Penfield, about eleven months after the first painful seizure. Ether was administered by the intranasal method. There was some handling of the vagus, but no change in pulse rate was noted at these times. The middle and inferior sympathetic ganglia on the left side were exposed and their branches were cut or torn out. The superior cardiac nerve was cut and the left sympathetic chain was severed just below the superior cervical ganglion, the ganglion being left in place. The wound was closed.

An incision was made on the right side preparatory to operating on the right sympathetic chain. Suddenly, the heart rate increased and the pulse became weak. Respirations came at longer intervals and were gasping. Adrenalin was injected into the heart, but in spite of artificial respiration with a pulmotor, circulation and respiration ceased abruptly. In the opinion of the operator, death appeared to be due to sudden cardiac failure.

Necropsy was performed by Dr. Paige, two and a half hours after death, and was limited to the thorax. The heart weighed 340 grams. Except for a few small sclerotic plaques in both coronary arteries, often seen in persons of this age, the findings were negative. There was no narrowing of the lumen of the vessels. In the arch of the aorta were similar tiny yellow plaques, the largest only 1 or 2 mm. in diameter. Microscopic examination of the tissues was made by Dr. A. M. Pappenheimer. The heart muscle was normal. At one place, the intima of a section of the coronary artery was very slightly thickened. The intima of the aorta showed a small area of necrosis. The media, in its outer third, contained one small area of scarring with a few infiltrating leucocytes. There was no rupture of the elastic fibers. Microscopic examination of the sympathetic ganglia removed at operation was negative. Dr. Pappenheimer's final note states that, "the autopsy discloses no anatomical basis for the anginal attacks."

PROGNOSIS

In no group of cases is the estimation of life expectancy more difficult. The patients with coronary disease may die in their first attack, as did Thomas Arnold, the schoolmaster of Rugby, or like John Hunter, may survive for twenty years, "his life in the hands of any rascal who chose to annoy or tease him." Experience has stressed two points: first, extensive sclerosis of the coronary vessels may exist without cardiac enlargement or significant changes in the electrocardiogram; second, it is precisely in those patients in whom relatively little is to be made out in the heart on physical examination, that early, sudden, and unexpected death not infrequently occurs. This fact was well exemplified in the case of a man, sixty-five years of age, with paroxysms of pain on slight effort, localized to the midsternal region, of three months' duration. There was moderate retinal and peripheral sclerosis. The blood pressure was 126 mm. Hg. systolic; 74 diastolic. The heart was not enlarged and there was a short systolic whiff at the apex. An electrocardiogram showed inversion of the T-waves in Leads I and II. The clinical diagnosis was sclerosis of the coronary arteries. During the year following his first visit, he improved markedly, and was able to walk four or five blocks with only an occasional precordial twinge. He took an ocean voyage to the Barbadoes and on the steamer was entirely free from pain. On his return he went up the subway stairs without discomfort. The T-wave in Lead II became upright in the graphic records. Three weeks after an office examination, I was called hurriedly to the Pennsylvania Railroad Terminal. He was going on a holiday to Atlantic City with his wife and while standing at the ticket window, purchasing his accommodations, fell over dead. Necropsy was not performed.

On the other hand, there is a group of patients with enlarged heart and electrocardiographic signs of serious myocardial damage, who survive their cardiac disability to die of another cause. For example, a man sixty years of age likewise suffered from attacks of pain induced by effort. The heart was markedly enlarged; there was no hypertension. The retinal and peripheral arteries were distinctly sclerosed. A large series of electrocardiograms showed persistent intraventricular block, with varying T-wave changes and occasional ventricular premature beats. He took several trips to Europe and continued his business as a stock broker, though never free from discomfort, taking nitroglycerin several times each day. Six years after the onset of his symptoms, he had a cerebral hemorrhage in bed during the night and died within twenty-four hours without regaining consciousness.

TREATMENT

If pain be regarded as an expression of a disturbed functional or structural state, therapy must be directed toward correcting or alleviating the basic disorder. When possible, this is the plan generally followed in medical and surgical practice; it is the logical procedure when the pain originates in the heart. A detailed account of the management of patients suffering from the various conditions which give rise to cardiac pain is not within the scope of this essay. The attempt to induce symptomatic relief through surgery of the cervical sympathetic chain merits, however, a word of comment.

Operative treatment of cardiac pain was proposed by François Franck in 1899 and first carried out by Jonnesco in 1916. Cutler[20] has recently summarized the experience up to 1927. At the Presbyterian Hospital, only five patients have had cervical sympathectomy, and reports of a sufficient number of accurately observed cases are not available in the literature to justify dogmatic conclusions. Thus far, the results have been variable and, on the whole, disappointing. One reason for lack of uniformity has been the fact that different observers have operated upon patients with pain associated with many different clinical conditions. It is generally conceded that patients with coronary disease are poor subjects for surgery, and it is in this group that the worst sufferers are found. Many of the cases reported as cured after sympathectomy have been followed for only a short time; others undoubtedly would have improved under medical treatment, provided an accurate diagnosis had been made. Until more is known concerning the mode of production of pain and its sensory pathways from the heart, the operation should be performed only on patients who suffer intensely, who have not improved under well-directed medical care and who, in the opinion of the physician, will stand surgical therapy without undue risk. These patients should be thoroughly studied both before and after sympathectomy. Detailed follow-up records, kept

over a period of years, will afford a basis for judgment as to its value. It is my present opinion that this operation will prove to have a very limited field of usefulness.

The paravertebral injection of alcohol into the posterior nerve roots has recently been advocated.[21] It is an uncertain procedure, unaided by visual guidance, and not without hazard. Richardson and White,[22] on the basis of a limited experience, have expressed the belief that alcohol injection is superior to sympathectomy. The relief afforded in some instances may well be due to blocking of cutaneous impulses, analogous to the results of skin infiltration with novocaine in the areas of cutaneous hyperalgesia, as practiced by Weiss and Davis.[23] Such cutaneous injections give prompt but only temporary relief in certain cases.

SUMMARY

The "disorder of the breast" described by Heberden, in the light of increasing experience, has proved to be the symptomatic manifestation of many pathological states. Perpetuation of the name originally given to the condition, and the concept of angina as a clinical entity, has resulted in confusion and disagreement as to its precise meaning. It is, therefore, suggested that the term "angina pectoris" be abandoned. Correlation of clinical and pathological data has demonstrated that cardiac pain may be associated with a variety of structural and functional changes. Pain resulting from disturbances in the region of the heart is best described as *cardiac pain*. In making a complete cardiac diagnosis, this should be qualified by a statement as to the probable structural and functional changes with which the pain is associated. Further knowledge concerning the mechanism of pain production may point the way to a more precise terminology. The conception of pain as a symptom will make for better diagnosis, for rational therapy, and for more accurate prognosis.

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PAIN DUE TO TEMPORARY OCCLUSION OF THE CORONARY ARTERIES IN DOGS*

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PORTER[1] stated that ligation of the coronary arteries in the dog did not produce pain. Smith also failed to observe pain in similar preparations. We do not believe, as do these investigators, that these observations offer convincing evidence against the coronary theory of pain. The occlusion was produced under anesthesia. Following severe thoracic surgery, an animal is depressed for hours and shows little evidence of pain that he may be suffering. Moreover, the pain of coronary occlusion may be transient. Until sudden occlusion of the coronary arteries has been produced in the conscious dog, one cannot conclude that the process is without pain.

Two years ago we began to study the effects of sudden coronary occlusion in conscious dogs. Observations made upon the pain response are herewith presented.

METHODS

The operation was performed under ether anesthesia by intratracheal insufflation (Meltzer[5]) and no other medication. The chest was opened by a transverse incision in the third or fourth intercostal space, carried from one side of the chest to the other, dividing the sternum. A rib spreader was inserted and a splendid exposure obtained. The pericardium was opened freely and the coronary arteries were exposed by dissection at the base of the heart. A thread of vaselined heavy linen was passed under each coronary artery within a centimeter of its exit from the aorta. In experiments where only the branches of the left coronary artery were to be studied, separate threads were passed under the vessels immediately after the bifurcation. The threads were attached to special devices for occluding the vessels and the chest was closed securely, after taking care to avoid partial pneumothorax. The devices for vessel occlusion were of two types. In some experiments the coronary traction threads were fastened to the end of a specially prepared camera shutter release, which protruded from the chest at the wound and was arranged in such a manner that by pressing the release, a short bar, through which the thread had been led, pressed firmly upon the artery. This method prevented interference with the heart itself, as would occur with direct pull upon the coronary vessel. A second method was that of

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attaching the traction threads to a suitable wire which was introduced into the thoracic cavity from a stab incision in the base of the neck. Traction upon the wire exerted traction upon and occlusion of the coronary vessels with minimal disturbance to the heart because of the axial direction of the pull. By either method the arteries could be occluded or released at will. In our earlier experiments we adhered diligently to asepsis but later abandoned it as unnecessary, since the animals were in good condition for experimentation within a few hours after operation. Three to four hours after the operation pain responses were studied. In some animals the pain response was so marked as to interfere with the electrocardiographic curves and morphine was given for this part of the experiment.

RESULTS

Fifty dogs were used. Ten were not fully conscious at the time coronary occlusion was produced and pain response could not be depended upon. Of the remainder the following examples are typical:

Protocol.—Mongrel dog, medium size. A traction thread was placed on the left anterior coronary artery immediately below its bifurcation and attached to a shutter release. Three hours later the animal was fully awake and lying quietly with E. K. G. leads attached. Vessel was suddenly occluded. Dog immediately howled and struggled. The vessel was released and dog became quiet at once. Repetition twice obtained the same results. Morphine phosphate, gr. ⅛, was given by hypodermic injection. Fifteen minutes later coronary artery was again occluded. Dog howled less vigorously and moved left fore-leg and paw. The vessel was released again with cessation of pain response. Repetition procured the same effect.

Protocol.—Mongrel dog of medium size. Traction threads were placed around each coronary artery near its origin and attached to the wire device. Four hours later the dog was fully awake and was connected to the E. K. G. leads. Gentle traction on left coronary artery. Dog uttered sharp cries, struggled, and attempted to arise. After 25 seconds vessel was released and animal became quiet at once. Gentle traction on right ligature obtained the same response. Several repetitions. Occlusion, then, of both vessels simultaneously produced the same type of symptoms but more violent. After two minutes of occlusion of both vessels ventricular fibrillation began, the pain response ceased, and death occurred from heart failure.

Most of the dogs responded similarly to these. In the majority of cases in which both coronaries were occluded simultaneously the heart did not fibrillate. Some of the dogs were less active and responded to occlusion by whimpering and weakly "purposeful escape movements." Body movements due to pain were easily distinguished from others, especially from asphyxial convulsions and other automatic responses, by their purposeful nature. The ten dogs that gave less clear-cut responses had survived the operation poorly or had been kept too long before being tested.

Electrocardiograms of all animals were taken and will be reported later.

SUMMARY AND CONCLUSIONS

It is pointed out that previous investigators have failed to get pain response in dogs following coronary occlusion, possibly because the animals had adjusted themselves to the altered cardiac condition by the time they recovered sufficiently from the anesthetic and surgical insult.

The detection of pain in these experiments was made possible by avoidance of anesthesia at the time of coronary occlusion. Acute severe pain was produced in forty out of fifty dogs by sudden occlusion of either coronary artery or of either or both branches of the left coronary artery, the pain beginning almost instantly after occlusion, lasting throughout occlusion, and ceasing immediately with release of the occlusion. When both coronary arteries were occluded simultaneously, similar responses resulted except that in a few cases ventricular fibrillation and death resulted. The ten dogs that gave less clear-cut results were not sufficiently alert to respond properly.

The responses are due to real pain and not to cardiocirculatory failure and asphyxia.

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THE RELATION OF CLINICAL, INCLUDING ELECTROCARDIOGRAPHIC, PHENOMENA TO OCCLUSION OF THE CORONARY ARTERIES BASED ON THE OBSERVATION OF A CASE*

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THE nature and origin of cardiac pain are still unsettled. The first contribution on this subject, made by Heberden[1] in 1768, emphasized, in describing the symptom complex which he called "angina pectoris," as the outstanding phenomenon "a painful and most disagreeable sensation in the breast" which affects persons while "walking and more particularly when they walk soon after eating." It does not cause breathlessness and stops on standing still. Sudden death was its other feature. Heberden saw no autopsies and refrained from associating these phenomena with any lesion. In 1776, Edward Jenner, in a letter to Heberden regarding John Hunter[2] and in another to Parry,[3] first suggested the association of angina pectoris with disease of the coronary arteries. He came upon this notion from post-mortem examinations of the hearts of persons who had been subject to such attacks. By 1799, Parry,[3] although he discussed the relation of anginal attacks to exertion, did not think that exertion was a necessary part of the symptom complex and did not include it in the formulation of his definition of angina pectoris. Nor is mention made one hundred years later of exertion in the "definition" of angina pectoris in Romberg's,[4] Strümpell's[5] or Osler's[6] textbooks. Allbutt[7] has this to say: "That the moments of the several seizures are often determined by effort, even by effort of mind or emotion, we know only too well; so well indeed that there is a notion abroad—one which more than once has been mentioned to me in discussing a diagnosis—that attacks are always so determined. Huchard countenanced this erroneous notion. Yet from Heberden himself we have learned that attacks may occur during sleep, often during rest."

In the course of the century a change in the meaning of the term originally proposed by Heberden has obviously taken place. In attempting to understand the history of ideas such as this, it would be interesting to learn how this change came about, but we have not searched the literature to trace the sequence.

Herrick[8] in 1912 gave the first comprehensive statement of the clinical features exhibited by one class of patients who are subject to pain and in whom occlusion of a branch or branches of the coronary artery

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is the etiological factor. In spite of the accumulation of a vast literature on this subject since then, the pathogenesis is still far from clear. The minimum signs and symptoms upon which one may venture to make a diagnosis of coronary occlusion and to give and to estimate the state of the coronary vessels and of the heart muscle are not known. Nor is it clear how much stress to place upon cardiac pain alone in deciding whether a coronary accident has occurred or whether pain is caused by a more transient process, such as spasm. It is in order to contribute to this phase of the matter that the case of this patient is published. For this purpose his clinical course was sufficiently well observed and the pathological examinations at autopsy were sufficiently well made.

CASE REPORT

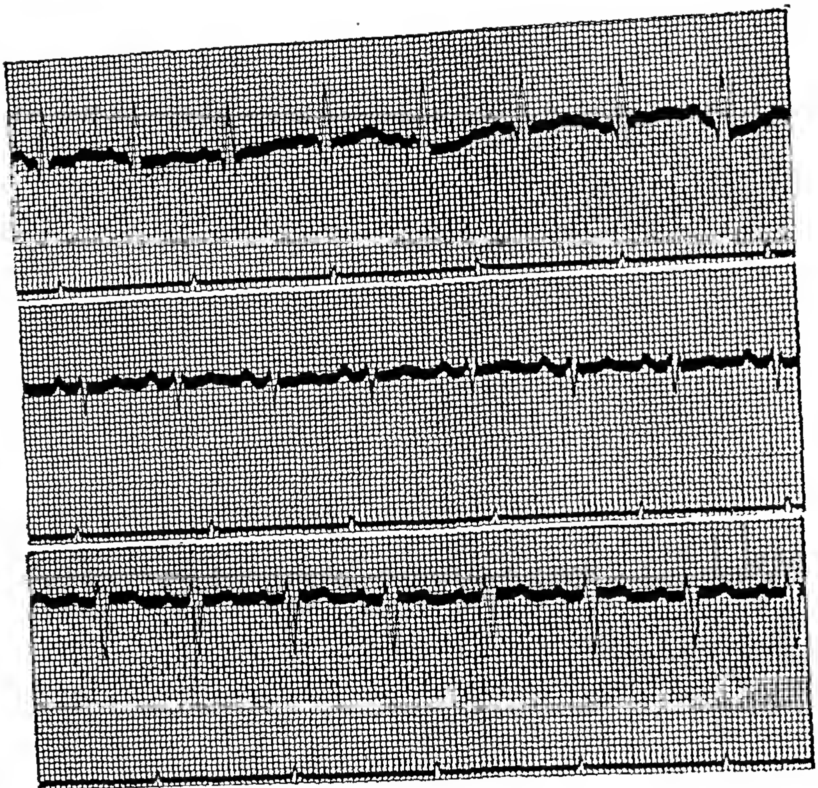
H. R., Hospital No. 4734, was a male, sixty-seven years old. He was admitted to the Rockefeller Hospital on April 4, 1923, having complained of shortness of breath for from eight to twelve months, swelling of the legs for eight months, tenderness in the region of the liver for from eight to twelve months and cough for one week.

The family history was negative.

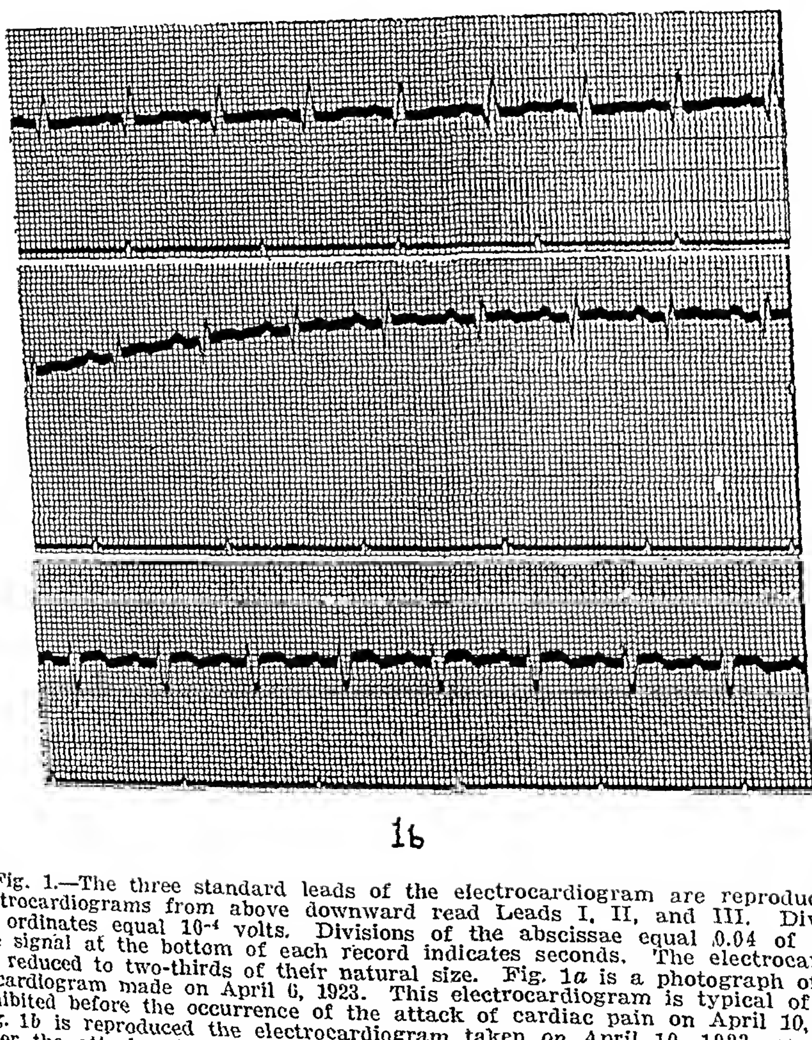
Past History.—There was no history of acute rheumatic fever, syphilis, or any other diseases having cardiac sequelae. He had enjoyed excellent health until the onset of the present illness.

Cardiac History.—In August, 1919, the patient was awakened at night with severe pain over the chest in front. He was so ill that he was unable to remember the character of the pain. He was too ill to be moved at once, but was taken to a hospital the following day. The pain continued for twenty-four hours. After four or five days 1000 c.c. of fluid were removed from the right pleural cavity by paracentesis. Following this treatment he improved and was discharged in two weeks. He felt weak and was unable to do what he wished. A year before admission to the Rockefeller Hospital he became short of breath on walking. Dyspnea gradually increased until he was forced to discontinue climbing stairs. Eight months before admission edema of the feet and legs first appeared. Shortly afterward tenderness in the right upper quadrant of the abdomen developed. Two months later he began to sleep on three pillows. Gradually all his symptoms, that is to say, dyspnea, edema, and tenderness of the liver, increased. From the onset of cardiac symptoms he received digitalis irregularly. The drug had not been given for several months.

Physical Examination.—The patient was an undernourished white man who lay propped up in bed and was orthopneic. Dyspnea was very marked when he attempted to lie flat. There was slight cyanosis of the lips. The temperature (rectal) was 100.7° F., and respirations 30 per minute. A tracheal tug was not felt. The heart was enlarged. The rhythm was regular, the rate 96 per minute. There were no thrills and no shocks over the precordium. The sounds over the base were clear. At the apex a soft blowing systolic murmur replaced the first sound. The murmur was not transmitted to the axilla. The radial vessels were thickened but were not tortuous. The systolic blood pressure was 130 mm. mercury and the diastolic, 85 mm. There was no capillary pulsation in the finger tips. Clubbing of the fingers was not present. There were signs of fluid in both pleural cavities. The liver was tender and was felt to within one finger's breadth of the umbilicus. There was pitting edema of the feet, ankles, and legs as far as the knees.



1a



1b

Fig. 1.—The three standard leads of the electrocardiogram are reproduced. The electrocardiograms from above downward read Leads I, II, and III. Divisions of the ordinates equal 10^{-4} volts. Divisions of the abscissae equal 0.04 of a second. The signal at the bottom of each record indicates seconds. The electrocardiograms are reduced to two-thirds of their natural size. Fig. 1*a* is a photograph of an electrocardiogram made on April 6, 1923. This electrocardiogram is typical of the form exhibited before the occurrence of the attack of cardiac pain on April 10, 1923. In Fig. 1*b* is reproduced the electrocardiogram taken on April 10, 1923, several hours after the attack. All the electrocardiograms taken afterward resembled this one. Not only are there changes in the form of the R- and S-waves, but the waves are of lower voltage.

The electrocardiogram showed a normal sinus rhythm. The conductiou time was normal and there was left ventricular preponderance.

The count of the red blood cells was 5,000,000. The hemoglobin (Sahli) was 97 per cent. The count of the white blood cells was 11,600, 65 per cent of which were polymorphonuclear in form. The phenolsulphonephthaleiu excretion was 65 per cent. The urea concentration index (Van Slyke index) was 36.7. The Wassermann reaction in the blood was negative. There was a trace of albumiu in the urine; in the sediment there were many leucocytes and epithelial cells.

Course in the Hospital.—During the first few days the edema decreased.

On April 10, 1923, he experienced severe precordial pain during the night. At 9 A. M. premature contractions were occurriug every fourth beat. Occasionally during auscultation there were runs of premature contractions, but when electrodes were applied, the irregularity was no longer present. The electrocardiogram showed splitting of the S-wave in Lead III (Fig. 1*b*). This wave had been sharply spiked in all the previous records (Fig. 1*a*). The voltage of the QRS complexes decreased. The conduction time increased from 0.16 to 0.18 of a second to from 0.20 to 0.21 of a second. There was no frictiou rub and no rise in temperature.

On April 13, the patient received digitan (Merck) 2.0 gm. by mouth within twenty-four hours. The ventricular rate slowed to from 70 to 80 per minute from having been between 90 and 100. The electrocardiogram showed further changes in the T-waves but no change in P-R time. There was no increase in the output of urine.

On April 18, 890 c.c. of fluid were removed from the right pleural cavity. Dyspnea was somewhat relieved. On April 19, during the morniug, 610 c.c. of fluid were removed from the left pleural cavity. At 3:30 P. M. the patient was sitting in bed talking to his wife. Suddenly he fell back against the pillows gasping for breath. There was marked cyanosis. The ventricular rate was from 35 to 40 per minute and the rhythm seemed to be regular. There was no pulse deficit. He was unable to speak. Respiratious became slower and more labored; cyanosis increased. The patient died within five minutes of the onset.

Summary.—The patient was admitted to hospital with fairly marked heart failure. In the absence of a history of acute rheumatic fever and of syphilis (the Wassermann reaction was negative) and in the absence of hypertension or of valvular disease on examination, we were of the opinion that senile changes had taken place in the heart muscle accompanying changes in the arteries. He had suffered from only two attacks of cardiac pain. The first attack occurred three and a half years and the second nine days before death. *Both attacks occurred at night while the patient was sleeping,* that is to say, they were not associated with exertion. Electrocardiographic data are not available for the first attack of pain; the second attack, however, was followed by certain changes (notching and decrease in amplitude) in the ventricular complexes of the electrocardiogram. Fluid was removed from both pleural cavities. Digitalis slowed the ventricular rate and gave characteristic changes in the T-waves of the electrocardiogram. There was no diuresis, however, following its administration. The patient was apparently slowly improving when he suddenly died. The diagnosis* was: *Etiological:* arteriosclerosis; *Anatomical:* cardiac hypertrophy, myocardial degeneration, coronary thrombosis, left ventricular preponderance; *Physiological:* normal sinus rhythm, relative mitral insufficiency, congestive heart failure.

SUMMARY OF AUTOPSY FINDINGS

The autopsy was performed by Dr. Arnold Branch an hour and a half postmortem.

*This diagnosis conforms to the nomenclature for cardiac diagnosis approved by the American Heart Association. AM. HEART J. 2: 202, 1926-27.

Anatomical Diagnosis.—Extreme thrombosis and atherosclerosis of the left coronary artery, focal thrombosis and atherosclerosis of the right coronary artery, myocardial degeneration, healed and recent myocardial infarcts, adherent pericardium, fibrous pleurisy, anthracosis, emphysema, arteriosclerosis, venous stasis of the liver, perisplenitis and perihepatitis, abdominal adhesions, hyperplasia of the spleen, arteriosclerosis of the kidneys, infarcts of the kidneys.

Gross Examination.—The body was that of a well-developed white man. The skin was pale and dry.

Thorax.—The lungs were voluminous. The precordial area was large. The right pleural cavity was almost completely obliterated by firm fibrous adhesions. The left pleural cavity was free except for fibrous adhesions in a small area laterally and posteriorly. There were a few bands between the left border of the pericardium and the lung, involving both the visceral and parietal layers of the pleura.

Lungs.—The lungs were moderately anthracotic and emphysematous. On section they were pale and spongy; they showed no gross lesion. The peribronchial glands were moderately enlarged and anthracotic. There was a moderate degree of atheromatous thickening in the larger branches of the pulmonary artery.

Pericardium.—There was a moderate amount of fat around the parietal pericardium. This layer was attached everywhere to the visceral layer by loosely adherent fine fibrous tissue. When the parietal layer was stripped back, it exposed a purplish brown surface over which were scattered small hemorrhagic areas. These were especially clustered around blood vessels.

The *heart* weighed 530 gm. The wall of the *left ventricle* measured 16 mm. in thickness at the base, 15 mm. at the level of the papillary muscle, and 4 mm. at the apex. The muscle was brownish-red and firm. The cavity was large, especially at the apex, the muscle there being thinned out and scarred. This thinning occurred abruptly. The papillary muscles were slender. The endocardium, in which there were scattered yellow patches of thickened endothelium, was pale brown. Scarring of the deeper layers produced a mottled appearance. One dark purple area about 3 cm. in diameter (Fig. 2*a*) occupied the base of the posterior papillary muscle. It was probably a recent infarct. The yellow scars occurred in greatest number in the apex, in the interventricular septum, under the aortic valve, and at the junction of the chordae tendinae with the papillary muscle (Fig. 2*a*). By far the largest irregular yellow area (3 cm. by 3 cm.) was situated partly in the anterior wall and partly in the septum midway between the apex and the base and just below the large left anterior descending branch of the coronary artery and differed from the other areas in that on cutting it definite scars were seen in the underlying muscle, the yellowish appearance not being due merely to thickened endocardium.

The wall of the right ventricle measured 6 mm. in thickness at the base, 7 mm. at the level of the papillary muscle, and 4 mm. at the apex. The muscle was firm and brown, but there was more epicardial fat than on the left ventricle. The papillary muscle and the cavity were not large. The endocardium was thickened in only three small places, two being on the anterior wall and the third on the septum.

The endocardium of the *left auricle* was slightly but definitely thickened and wrinkled. The wall measured 4 mm. in thickness. The cavity was not enlarged.

The endocardium of the *right auricle* was thickened around the orifices of the venae cavae. It was smooth throughout. The thickness of the wall was from 2 to 3 mm. The cavity was not enlarged.

Mitral Valve.—The mitral ring measured 8.5 cm. No stenosis was present. The lateral cusp was slightly thickened only at the line of closure. The aortic cusp showed yellow thickening at the base and more marked thickening near the free edge with a narrow transparent zone between. It was covered with endothelium

a

b

Fig. 2.—In Fig. 2*a* is presented a photograph of a colored drawing of the cavity of the left ventricle. A recent infarct in the regions of the posterior papillary muscle is readily identified by the dark area. The whitish areas are due to thickening of the endocardium. Scarring at the apex and thinning of the muscle here are to be noted. In Fig. 2*b* is shown a photograph of a colored drawing of the left coronary artery and its branches.

throughout. Along the line of closure, which was but slightly thickened, there was a reddish discoloration. A series of tiny nodules occurred at the junction of the chordae tendineae.

The leaflets of the *tricuspid valve* were mobile. The ring measured 12.7 cm. There was no thickening.

The *aortic valve* was well preserved; there was only slight thickening of the endocardium in the right posterior cusp and on the interventricular septum below the valve at its junction with aortic cusp of the mitral. Nowhere was there calcification. The opening measured 5.4 cm. in circumference.

There was no abnormality of the *pulmonary valve*. It measured 6.6 cm.

At its origin the *right coronary artery* showed definite hard thickening for a few millimeters of its length, but the vessel was patent. It then appeared normal for a short distance. At the point where the first noticeable branch to the auricles and pacemaking area was encountered there was a marked yellow thickening; the orifice of this small artery was narrowed, but in the rest of its extent, as far as it can be traced to its finer terminations, the walls were thin and elastic and the lumen was patent. The whole of the *right circumflex artery* appeared normal with the exception of a few scattered small yellow plaques. The *posterior descending branch* was normal until a point was reached in its course down the posterior wall of the left ventricle, just above its final bifurcation into the two terminal arteries. At that point the wall was thickened, firm, calcareous, irregular and bead-like, and the lumen could not be seen. Below this occlusion, which was about 0.5 cm. in length, the artery again appeared normal. The lesions just described appeared to be old, but it is quite possible that a very small recent clot might have sufficed completely to block it.

The *left coronary artery* (Fig. 2*b*) immediately divided into three branches, namely, the large *left anterior descending branch*, a fairly large *marginal branch*, and a quite well-developed *left circumflex branch*. At its orifice it was thickened, but the lumen was patent. The wall of the left anterior descending branch was so firmly calcified that it was cut only with difficulty; the lumen was apparently blocked throughout by a yellow gelatinous clot. This artery lay over the area of extensive scarring seen on the internal aspect of the left ventricle. The *marginal branch* was completely blocked about 1.5 cm. from its origin by a reddish thrombus; the artery after this point was very firm and thickened. Below this it again became patent and appeared normal. The *left circumflex branch* was blocked by a red thrombus. The walls were thickened *until* it branched into smaller arteries on the posterior surface. These smaller branches appeared normal.

The *aorta* was slightly thickened in the sinuses of Valsalva and around the coronary openings. In the arch and in the lower abdominal aorta there were fairly marked atherosclerotic changes. In the thoracic portion these occurred as localized thickenings covered by endothelium which were especially marked around the orifices of the intercostal vessels. At the lower end, however, there were plaques of calcification and ulceration.

The larger branches of the *pulmonary artery* in the lung showed a slight degree of sclerosis.

The *spleen* weighed 110 gm. In the capsule which was attached to the diaphragm by fibrous adhesions were localized thick yellow plaques. There were no infarcts to be seen.

The *adrenals* were well preserved and large. The pancreas was pinkish-gray in color.

The *left kidney* weighed 130 gm. The capsule could be stripped with slight difficulty. On section the cortex was wide; the medulla, pale. Differentiation of cortex and medulla was not sharp, but the kidney appeared very well preserved. In the cortex at the lateral border was a small firm yellow area of infarction.

The pelvis and ureter were intact. The *right kidney* weighed 120 gm. It was similar to the left, except that there were no infarcts.

The *liver* weighed 1320 gm. The capsule appeared thickened along the inferior surface of the anterior border. It was yellowish-red and mottled. On section it exuded blood. The markings were fairly distinct; the substance was friable.

On section of the *brain* there were no areas of hemorrhage to be seen, and the blood vessels at the base showed no evidence of atherosclerosis.

MICROSCOPICAL EXAMINATION

Coronary Arteries.—Sections were examined from the main branches of the left coronary artery, that is to say, the left anterior descending, the left marginal, and the left circumflex. The lesions in all were identical. The adventitia was intact, the media narrow, and the intima thickened. The elastic tissue stain showed this quite definitely. The lumen was obliterated by healed canalized fibrous tissue in which there were a few pigment-containing cells but no inflammatory exudate (Fig. 3). The areas of canalization were relatively small in comparison with the fibrous tissue and in no wise approached the cross-section of the lumen of the vessel if it had been normal. These small vessels varied in size from capillary diameter to that of small arterioles. They numbered from five to over a dozen in the various sections. A few contained red blood cells and appeared patent while the majority were filled with pink staining, homogeneous hyaline-like material, not taking the characteristic fibrin stain. In a few this pink tissue formed a thick ring around the lumen. One could imagine that only a few were patent. This appearance was due to healed canalized thrombi; there may have been recent thrombosis.

Left Ventricle.—In none of the sections was there evidence of active inflammation. The section from the posterior wall showed areas of fibrous scarring. The muscle fibers were large and contained large nuclei; distinct striations and contractile elements were present. In a section from the region of the anterior papillary muscle a similar condition was observed. In the septal area definite discrete fibrous intimal thickening was noted, the tissue being relatively acellular. The posterior papillary muscle was the locus of a recent infarct (Fig. 2*a*); the musculature was infiltrated with red blood cells and a few white blood cells. The muscle tissue here too appeared rather homogeneous and striations were less distinct. In a section from the apex the wall was thin (Fig. 2*a*), and the pericardium was thickened and adherent. The endocardium was thickened, and there was marked fibrosis and replacement of the muscle tissue. There was in short, endocardial thickening, fibrosis, and recent infarction. A section from the lateral wall of the *right ventricle* showed no change from the normal.

The endocardium of the *left auricle* was slightly thickened. One vessel showed evidence of fibrous thickening. There was definite thickening, fusion, and hyalinization of the pericardium of the *right auricle;* there was sparse perivascular small round cell infiltration in the parietal layer.

Aorta.—The adventitia was normal, as was also the media. The intima was irregularly thickened and deep in its substance were areas made up of pale staining acellular necrotic tissue. The section included the origin of a small vessel, and at this point blood appeared to have welled into a space in the intima raising the surface layers. At no place was there ulceration. The appearance was that of atherosclerosis.

The *medullary* vessels of the *kidneys* were engorged as were also the glomerular tufts. The vessels were rather thickened; there was an occasional tuft with perivascular fibrous thickening. Small infarcts were seen in the cortex just under the capsule; these were infiltrated with small round cells. In infarcts which were larger but still microscopical in size there were whole areas of tubular and glomer-

ular tissue which had undergone necrosis. The vessels in the vicinity were congested; around the thrombosed vessels causing the infarct there was hemorrhagic extravasation. In Regaud-fixed tissue mitochandria had disappeared. There were present then infarction and atherosclerosis (slight).

Liver.—There was early cyanotic atrophy. The capsule was slightly thickened, and there was subcapsular fibrosis. The appearance was that of venous stasis.

Lungs.—There was fibrous thickening of the pleura and anthracosis. There were pigmented mononuclear phagocytes in the alveoli.

Fig. 3.—In this figure is reproduced a microphotograph of a cross-section of a branch of the left coronary artery. For description see text. Magnification 42. (? reduced.)

Spleen.—There was perisplenitis. The capsule was infiltrated with cells, the sinuses were filled with blood, the pulp was not hyperplastic. The blood vessels were thickened. The malpighian corpuscles were numerous.

Summary.—The chief interest at autopsy was found to lie in the heart. Both healed and more recent infarcts of the left ventricle and septum were found. The apex was very thin and scarred. In the coronary vessels supplying the left ventricle were areas of calcification and thickening, and on section the lumen of the

vessels appeared to be completely closed. The healed thrombi were pierced by small canalized vessels. The area of scarring in the heart muscle corresponded to the areas supplied by the vessels which were occluded by the canalized thrombi.

DISCUSSION

The clinical and post-mortem findings of a patient dying of coronary occlusion have been presented. From examination of the heart at autopsy there is no doubt that the patient had suffered from infarcts in the heart on many occasions. These had apparently occurred without causing conspicuous symptoms. There was nothing in the history, physical examination, or electrocardiographic record that led to the suspicion that the patient had been the subject of such grave changes in the myocardium and coronary vessels as were found at autopsy. There were only two attacks of cardiac pain; the first occurred three and a half years before admission to this hospital, and the second nine days before death. Both of these attacks came on at night while the patient was asleep. They occurred obviously *without physical exertion.* Following the last attack of severe cardiac pain, there occurred the only disturbance of cardiac rhythm of which we have knowledge. There were none of the usual signs associated with coronary thrombosis, such as rise in temperature or pericardial friction rub. The only indication appropriate to the lesion which the autopsy disclosed was the count of the white blood cells which rose from 11,600 (April 8) to 16,400 (April 12) and fell later to 10,800 (April 14). According to Wearn,[9] however, the classical signs of coronary occlusion may not appear when it occurs in the presence of heart failure. Friction rub may have been absent because the pericardium was adherent. At autopsy there was a fresh infarct in the left ventricle, at the base of the posterior papillary muscle corresponding to a region supplied by the circumflex branch of the left coronary artery. The cardiac pain from which the patient suffered nine days before death may have been due to the occurrence of this infarct. On the other hand it may have been of more recent origin. Evidence that damage to the cardiac muscle had occurred after the time of the cardiac pain on April 10, was shown in the electrocardiogram (Figs. 1*a* and 1*b*) by splitting the S-wave in Lead III. There are, of course, corresponding changes in Lead II. Here the R-wave was followed by a somewhat deeper S-wave. After the attack of cardiac pain the sequence of these waves was, however, reversed (Fig. 1*b*) and the ventricular complex was opened by a negative followed by an approximately equal positive swing. These changes indicated without a doubt change in the path of the excitation wave. There occurred also decreases in amplitude of the QRS complexes (compare Figs. 1*a* and 1*b*). Smith[10] has called attention to this occurrence following occlusion of the left coronary artery, especially when the circumflex branch is involved either alone or with the ante-

rior descending branch. According to this observer this change is found with less frequency, however, than are alterations in the T-wave. None of the changes in the T-wave, such as have been described by Herrick[11] and by Pardee,[12] were seen. The autopsy, nevertheless, revealed lesions in branches of the left coronary artery which, according to the experiments of Smith and reports of cases by Herrick, Pardee and others, are the occasion of such changes in the electrocardiogram. The lesions were due as has been stated to extensive arteriosclerotic changes. All three branches of the left coronary artery were profoundly involved, a recent infarct occurring in a region supplied by the circumflex branch, while the right one was less affected. In all of them there were old thrombi which had become canalized. In some, however, the thrombi were of more recent origin. It is difficult to see how an adequate blood supply to the heart muscle was maintained under these circumstances. The heart muscle can, of course, have been nourished by way of the thebesian vessels. Wearn,[13] in the light of recent studies, thought that in the event of gradual closure of the orifices of the coronary arteries, the thebesian vessels can supply the heart with sufficient blood to enable it to maintain an adequate circulation. It is impossible to decide whether death was due to gradual closing off of the blood supply by thickening of the intima and thrombus formation until a state was finally reached where the supply of blood was inadequate, or to sudden complete blocking of the circumflex branch of the left coronary artery which caused the infarct in the region of the posterior papillary muscle. If, however, the infarct occurred nine days before death and was the occasion of the cardiac pain experienced by the patient at that time, it is possible to connect the occlusion of the circumflex branch of the left coronary artery with the electrocardiograph changes which were then observed. No attempt has yet been successful, however, in correlating specific changes in electrocardiogram with injury to special coronary vessels. The time has come, perhaps, when an effort should be made to recognize certain distinctions. It is to be expected that when occlusion (and by this is meant the acute lesions, not the slowly developing senescent process*) takes place, fever, leucocytosis, and pain occur, irrespective of the branch of the coronary artery which is involved. To identify the branch that is occluded, a relation should be shown to exist between the change in the electrocardiogram and pericardial friction rub on the one hand and the exact vessel occluded on the other. In examining the reports of the published cases it has not been possible in most instances to obtain such information in order that it might be arranged in a way to correlate sign and pathology. In searching the literature, as has been said, only those cases have been sought in which an acute

*How the slowly developing senescent process terminates is scarcely known. It may include a transition between gradual narrowing and sudden occlusion, when a condition simulating an acute lesion may appear.

TABLE I

SUMMARY OF CASES IN WHICH OCCLUSION OF A CORONARY ARTERY WAS DEMONSTRATED AT AUTOPSY EXAMINATION AND IN WHICH ELECTROCARDIOGRAPHIC REPORTS ARE AVAILABLE

AUTHOR	REFERENCE	PATIENTS	AGE IN YEARS	EXPERIMENTS	SYMPTOMS	EXERTION AS EXCITING CAUSE	SIGNS	COEXISTING ELECTROCARDIOGRAPHIC CHANGES		CORONARY ARTERY FOUND TO BE INVOLVED AT AUTOPSY EXAMINATION
								DECREASE QRS	T-WAVE NEGATIVE	
Herrick	J. A. M. A. 72: 387, 1919	Case 3	42		Substernal pain, tachycardia	Not known	Not given	+ (178 days after occlusion)	+ (T_2 and T_3 41 days after occlusion)	Descending branch of left coronary artery; also the circumflex branch by old thrombi
Smith	Arch. Int. Med. 32: 497, 1923	Case 1	44		Stab wound				+ (17 days after ligation)	Ligation of descending branch of left coronary
		Case 3	51		Substernal pain	0	Not given	+ (11 days after pain)	+ (11 days after pain)	Descending branch of left coronary and also two branches of the circumflex branch; died 11 days after pain
		Case 5	39		Pain, nausea and vomiting	?	Friction rub	+ (2 weeks after onset)	+ (2 weeks after onset)	Descending branch of left coronary; died 2½ months after pain, infarct healed
Herrmann	J. Missouri M. A. 17: 406, 1920	Case 2	61		Pain	+	Friction rub, fever, leucocytosis	+		Thrombosis of descending branch of left coronary
		Case 6	53		Pain	0		+		Thrombosis of descending branch of left coronary

TABLE I—CONTINUED

AUTHOR	REFERENCE	PATIENTS	AGE IN YEARS	EXPERIMENTS	SYMPTOMS	EXERTION AS EXCITING CAUSE	SIGNS	COEXISTING ELECTROCARDIOGRAPHIC CHANGES: DECREASE QRS	COEXISTING ELECTROCARDIOGRAPHIC CHANGES: T-WAVE NEGATIVE	CORONARY ARTERY FOUND TO BE INVOLVED AT AUTOPSY EXAMINATION
Stewart	Case now being reported		67		Pain	0	Leucocytosis (no fever and friction rub)	+	0	Fresh infarct in area supplied by circumflex of left coronary artery which was occluded; died 9 days after onset of pain and Ekg. changes
Smith*	Arch. Int. Med. 22: 8, 1918			56 dogs 8 dogs					+ 0	Any branch of left Any branch of right
Smith*	Arch. Int. Med. 25: 673, 1920			14 dogs 5 dogs					+ 0	Descending branch of left and circumflex branch Right coronary
Smith*	Arch. Int. Med. 32: 497, 1923			records of 29 dogs of 1918 series (see above) restudied				+ in 100 per cent + in 20 per cent + in 30 per cent	According to 1918 report T-waves negative in all instances	Left Circumflex branch Descending branch of left coronary Left circumflex as well as descending branch of left coronary

*In the case of the experiments reported by Smith it is the artery which was ligated that is referred to in the last column.
+ = present
0 = absent

lesion was followed in turn by changes in electrocardiogram and then within a short time by autopsy examination. It is only in this way that specific electrocardiographic signs can be correlated with lesions in special coronary vessels (Table I).

Smith[10] found in dogs decreases in amplitude of the QRS complexes in all the cases when the circumflex branch of the left coronary artery was occluded alone, in 20 per cent when the anterior descending branch was occluded alone, and in 30 per cent when the anterior descending branch as well as the circumflex branch was involved (Table I). He cites 2 cases (Herrick's[11] and his own) in which comparable electrocardiographic signs were observed when there was occlusion of the left circumflex branch and also of the anterior descending branches, though the thrombi in the circumflex branches were of more recent origin. Pardee's case[12] unfortunately cannot be made to serve as evidence, since the patient recovered and the vessel involved is not known. His other published cases[14] cannot be utilized in this connection, since the patients died of heart failure and did not exhibit signs or symptoms associated with disease of the coronary arteries, although at autopsy alterations were found in these vessels. So far as can be ascertained death did not follow acute coronary occlusion. It is not possible in Wearn's 19 cases[9] to correlate the vessels involved with the electrocardiographic changes. He states, however, that the QRS complex was diminished in height in about one half, while in only one of them was the circumflex branch occluded. In the 2 cases of thrombosis of the descending branches of the left coronary arteries reported by Herrmann[15] the QRS complexes were diminished in height. It is not known whether the T-waves changed. In Willius'[16] cases the changes in the coronary vessels were of a chronic nature, and the cases do not fall in the group under consideration. In our case the recent infarct was found in the area supplied by the circumflex branch of the left coronary artery. This was occluded; correlated with this there was diminution in amplitude of the QRS complexes of the electrocardiogram. Other branches were involved to be sure, but there were no areas of recent infarction in the regions supplied by these branches. There may be, then, based on Smith's experiments, on Herrick's (one), Smith's (one), and Wearn's (one) cases and on our own, a rough correlation between occlusion of the circumflex branch of the left coronary artery and decrease in amplitude of the QRS complexes. But in one of Smith's, Herrmann's and most of Wearn's cases, exact correspondences are not to be found. If, in the future, observers will make specific statements about the occurrence of pain, exertion as the exciting cause, fever, leucocytosis, friction rub, and of changes in T-waves, QRS complexes, and rhythm of the electrocardiograms, and about the specific vessels found at autopsy to be involved in the acute coronary accident, then sufficiently accurate material will accumulate upon

which it will be possible to decide whether a closer correlation can be made between lesion and sign than is possible at present. Under the circumstances, then, exact correlation between lesion and electrocardiographic sign is impossible. Whether further refinements of study, either of the site of injury or of better definition of alterations in the electrocardiograms, will permit accurate diagnosis cannot now be known.

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THE ACTION OF DIGITALIS IN COMPLETE HEART-BLOCK

Its Toxic Influence on the Idioventricular Rate and Rhythm*

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THE limitation of treatment with digitalis in patients with complete heart-block is by no means established. Although the administration of the drug has in certain instances been accompanied by beneficial effects,[1, 2, 3, 4] in others it has been directly associated with grave arrhythmic accidents at times unfortunately ending fatally.[5, 6] It is such serious outcomes that have probably impelled competent observers to state emphatically "that safety demands that digitalis be avoided in any case with bradycardia."[7] Such overcautiousness, however, may deprive a patient with complete heart-block of the only remedial measure for the relief of distressing symptoms when heart failure sets in.

The main discrepancy in views seems to center on whether the beneficial results of the drug are due to an increase in the muscular contraction of the heart or to an augmentation of the automatic ventricular rate. It is held by some that a quickening of the slow idioventricular rate is a therapeutic result to be desired,[8] and an increase in rate has even been suggested as a possible indicator of the therapeutic effects of the drug.[9] It is claimed by others that a clinical improvement in patients with complete heart-block and decompensation has been demonstrable *only* after an increase of the idioventricular rate.[10]

From a study of 8 patients with complete heart-block and signs of heart failure who have been admitted to the wards of the Montefiore Hospital within the last two years and treated with tincture of digitalis, it has been concluded that the ventricular rate is increased appreciably only after the administration of large doses of digitalis; that is, doses that are greater than those commonly employed in therapeutics. Three of these cases are reported in detail, since each represents a distinct type of toxic digitalis action on the ventricles in complete heart-block. The increase in the ventricular rate following the administration of digitalis was accompanied in 2 patients by such distressing symptoms as breathlessness and fainting spells with visual disturbances and in 1 patient there were fleeting periods of total loss of consciousness, all of which passed away with the restoration of the dominant idioventricular rate and rhythm. In 2 of the patients, digitalis had the effect of initiating transient auricular fibrillation.

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REVIEW OF LITERATURE

It is well established from experimental observations on the mammalian heart that after the development of lasting auriculo-ventricular dissociation and complete heart-block following the destruction of the bundle of His, effective doses of digitalis may increase the slow rate of the idioventricular rhythm.[11, 12, 13, 14] It is possible to have a bigeminal rhythm or a rapid regular or irregular ventricular tachycardia of the independently beating ventricles depending upon the quantities of digitalis introduced into the circulation. In human beings, a notable increase of the dominant rate of the ventricles in complete heart-block in association with the administration of digitalis has not been observed except under unusual circumstances. In the majority of cases in which an attempt has been made to induce a change in the idioventricular rate by digitalis, no results could be obtained when therapeutic doses were used.[15, 16, 17] The few instances cited in the literature that are supposed to have shown positive changes deserve repetition.

Bachman[10] noted what he believed to have been a "conspicuous" increase in the ventricular rate, with a notable decrease in the auricular beat in a patient with complete heart-block following the administration of the tincture of strophanthus. His patient received 5 minims of the tincture three times a day for twelve days. Whereas before the administration of the drug, the ventricular rate averaged 23 beats per minute, a day later it had increased to 27 beats. On the sixth day of observation, after the dose had been doubled for the day, the ventricular rate of the patient was found to be 33 beats per minute. A careful review of Bachman's protocol reveals, however, that despite the persistent use of the drug in the doses mentioned, the ventricular rate was only 28 beats per minute at about the eighth day and remained at that level throughout the patient's period of observation. The total increase of the basic ventricular rate, therefore, did not amount to more than 5 beats per minute, which is, as will be later pointed out, a relatively normal variation in complete heart-block when the rate is counted over a prolonged period of time. Such small increments in the rate of the ventricles could be as well attributed to the variability of the inherent mechanism of the independently beating ventricles as to the action of the drug itself.

Meyer[6] recorded polygraphically a doubling of the ventricular rate in a patient with complete heart-block during the administration of the infusion of digitalis. In his patient the ventricular rate varied at first between 28 and 36 beats per minute and increased up to 70 beats per minute five days after medication was started. An analysis of his records, however, reveals that five days prior to the administration of the drug, the patient showed a totally irregular heart action with a ventricular rate of almost 80 beats per minute, which in the next few days gradually became more regular and decreased spontaneously

to an idioventricular rate that varied between 26 and 28. It is obviously impossible in so labile a rhythm as this case presents to attribute any definite acceleration of the automatically beating ventricles to the use of the infusion of digitalis. Besides, since there was no other adequate evidence of digitalization, and the patient died two days following the sudden increase in the ventricular rate, it is probable that the rise of the rate might have been an ante-mortem phenomenon, as has been observed in other patients with complete heart-block, independently of the use of any drug.[20]

Bastedo's case[5] is more convincing, although the increase in the ventricular rate of his patient was accompanied by the appearance of retrograde rhythm, a condition observed experimentally in the transition stages from partial to complete heart-block and usually considered as an index that the block is incomplete.[22] In his patient with heart-block, digitalis had the effect of bringing on short spells of doubling of the intrinsic rate of the ventricles with the onset of retrograde rhythm. In one of the polygraphic tracings from this case, the ventricular rate showed a jump from 26 to 54, the auricular rate dropped from 62 to 54, and the rhythm was reversed so that the auricular systole followed that of the ventricles instead of preceding it, both having the same rate at the end of each such paroxysm. There was a long pause of the ventricles lasting some seconds following this change. During such variations of rhythm, the patient experienced passing attacks of faintness or lightheadedness though lying flat in bed.

It should be mentioned here, that in all of the three cases cited above, the suggested increase in the rate of the ventricles as a result of digitalis administration has been deduced from polygraphic tracings. By such means it is difficult to ascertain whether the increase in the ventricular rate is due primarily to stimulation of the idioventricular pacemaker or to premature beats of the ventricles. In some such instances even electrocardiograms may be difficult to interpret.

CASE REPORTS

Case 1.—B. W., a woman, aged eighty-two years, was admitted to the Montefiore Hospital on September 26, 1927, and died on April 21, 1928. She complained of having had intermittent attacks of pain in the right upper quadrant for the past fifty years. Within the last two years she had been suffering from shortness of breath, precordial pains upon the least exertion, insomnia, headaches, and weakness.

Ten years ago (February, 1918) the patient was informed that she had gall bladder disease with gallstones but because of her age it was not thought advisable to operate upon her. With the exception of the periods when she experienced these recurrent attacks from her "gallstones," the patient was able to attend to her house duties until June, 1922, when she entered St. Luke's Hospital, complaining of a new series of symptoms which she developed in rapid succession. These were precordial pains, shortness of breath, and headache with weakness. The precordial pains came on with the least exertion and were paroxysmal in character. They were

accompanied by periods of restlessness and a sudden increase in respirations. During the seizures she would turn pale and cold and would be unable to speak. In half a minute after their onset she would feel better again but very weak. She remained at St. Luke's Hospital at first for about five weeks and after a short stay at home, had to be readmitted, when, because of the increasing severity and duration of her attacks and precordial pain, it was thought advisable to keep her in the hospital for the next fifteen weeks. She returned home but remained in bed most of the time during the following eight months.

In September, 1927, two weeks prior to her admission to the Montefiore Hospital, she had a very severe attack of pain over the precordial region for which she was treated at Bellevue Hospital. On the day of her admission to the Montefiore Hospital she had had a similar attack at home, but this time it was preceded and accompanied by loss of consciousness, convulsions, and incontinence of urine. It is not known whether her pulse rate was very slow during this seizure. She never had a similar experience during her entire period of stay at the Montefiore Hospital.

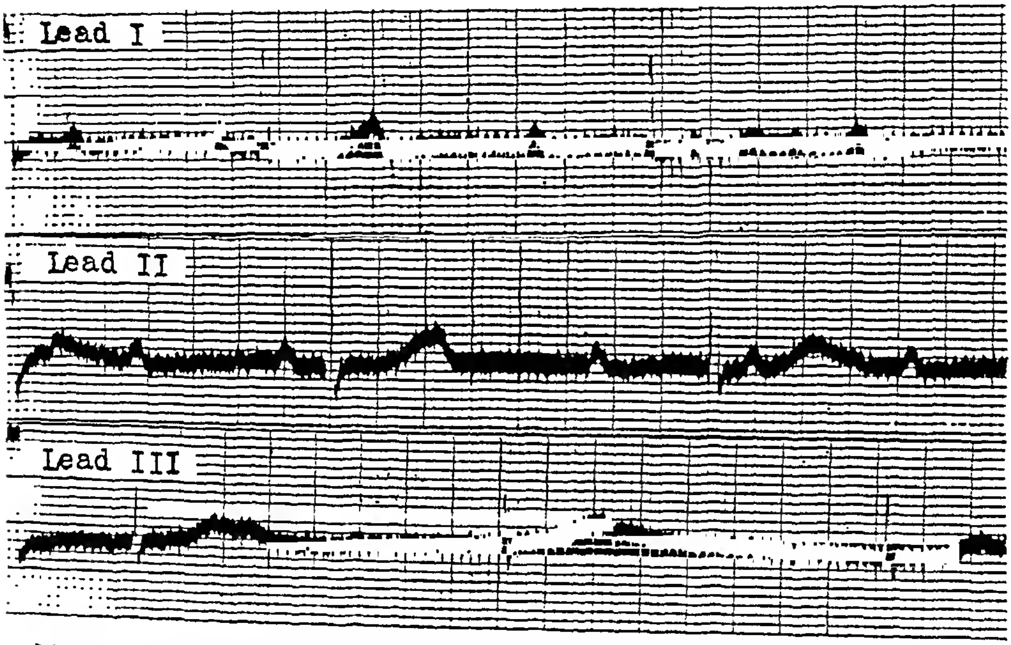

Fig. 1.—Case 1. Ecg. No. 3617. Jan. 4, 1928. Complete heart-block. Ventricular rate 37.3. Auricular rate 99. The ventricular complexes are all of the supraventricular form. The T-waves are all positive.

Physical examination revealed an old woman sitting in bed and reclining on several pillows. She was slightly dyspneic, but mentally clear. There was marked cyanosis of her lips, hands, and feet. The pupils were equal and both reacted to light and in accommodation. There was slight distention of the superficial jugular veins. The apical impulse of the heart was in the fifth intercostal space to the left of the midclavicular line. The heart rate was slow but regular and averaged 37 beats per minute. In the interventricular silences two auricular sounds could be heard near the fourth intercostal space to the left of the sternum. The aortic second sound was markedly accentuated. The pulses were equal and regular and of very good force. There was no pulse deficit. The radial arteries were thickened and slightly beaded. The blood pressure was 232/94 mm. It was the same on both sides.

Over the lungs posteriorly there was flatness, with absent breath sounds more marked on the right side than on the left. Many moist râles were heard over the extreme left base posteriorly. The abdomen was soft, lax, and there was a large

fluctuating and tender mass in the right upper quadrant. The liver edge was not palpable. There was no evidence of ascites. The lower extremities showed no edema.

Roentgen examination of the chest failed to reveal any abnormality of the lungs. The heart shadow showed slight enlargement of the left ventricle. The arch of the aorta showed a few calcific plaques.

The Wassermann reaction was negative on several occasions. The blood sugar was 106 mg. per 100 c.c. Urea nitrogen was 24.4 mg. per 100 c.c. The urine had a specific gravity of 1023, and there was no sugar or albumin; microscopic examination revealed a few pus cells.

Several electrocardiograms taken shortly after admission revealed the presence of complete auriculo-ventricular dissociation with complete heart-block, the ventricular rate averaging 37.3 beats per minute and the auricular rate being 99. There was

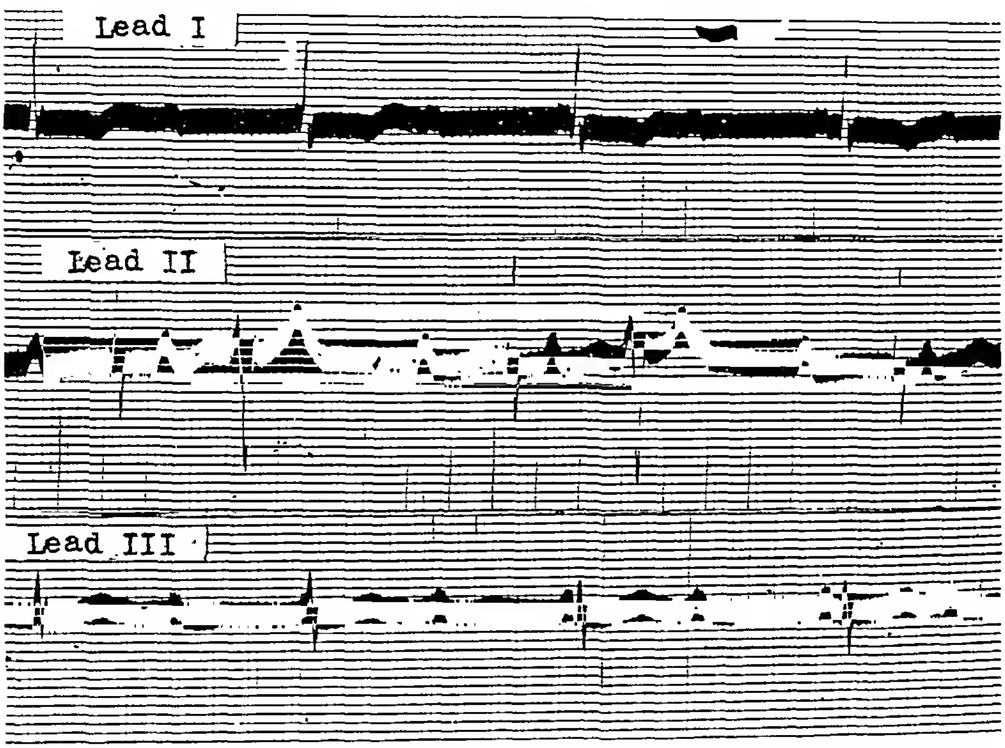

Fig. 2.—Case 1. Ecg. No. 3591. April 17, 1928, 10 A. M. Complete heart-block. Basic ventricular rate 48.4. Auricular rate 100. Lead II shows alternate premature beats of ventricle. T_1 is negative.

slight left axis deviation in some of the records. The ventricular complexes were all of the supraventricular form and the T-waves were all positive.

Course and Progress.—During her stay in the hospital the patient was able to be in a wheel chair for some of the time until March 14, 1928, when it was found necessary to perform thoracentesis of the chest which yielded 1500 c.c. of clear straw-colored fluid. From that time on, she was kept in bed, and an attempt was made to see if digitalis in adequate amounts would increase her idioventricular rate.

On March 27, 1928, the patient received orally 13 c.c. of the tincture of digitalis within twelve hours. (This was approximately a body-weight dose figured out by the Eggleston method.) She experienced no nausea or vomiting. An electrocardiogram taken on the following day revealed a slowing of the auricular rate from 99 to 78 beats per minute, but the ventricular rate remained practically unaffected,

showing an average of 35.3 beats per minute. There was definite evidence of digitalization in the electrocardiogram. The T-wave was negative in Lead I and reduced in size in both Leads II and III. P was now negative in Lead III. There were no significant changes noted in any of her electrocardiograms studied within the next few weeks, up to those taken on April 16, 1928, when the auricular rate showed a return to the original rate of 99 beats per minute and the T-waves had resumed their normal shape and size in every lead. (Fig. 1.)

On the morning of April 16, 1928, the patient complained of pain in the right side of her chest posteriorly near the angle of the scapula. Physical examination at this time revealed signs of dullness at the right base posteriorly, bronchovesicular

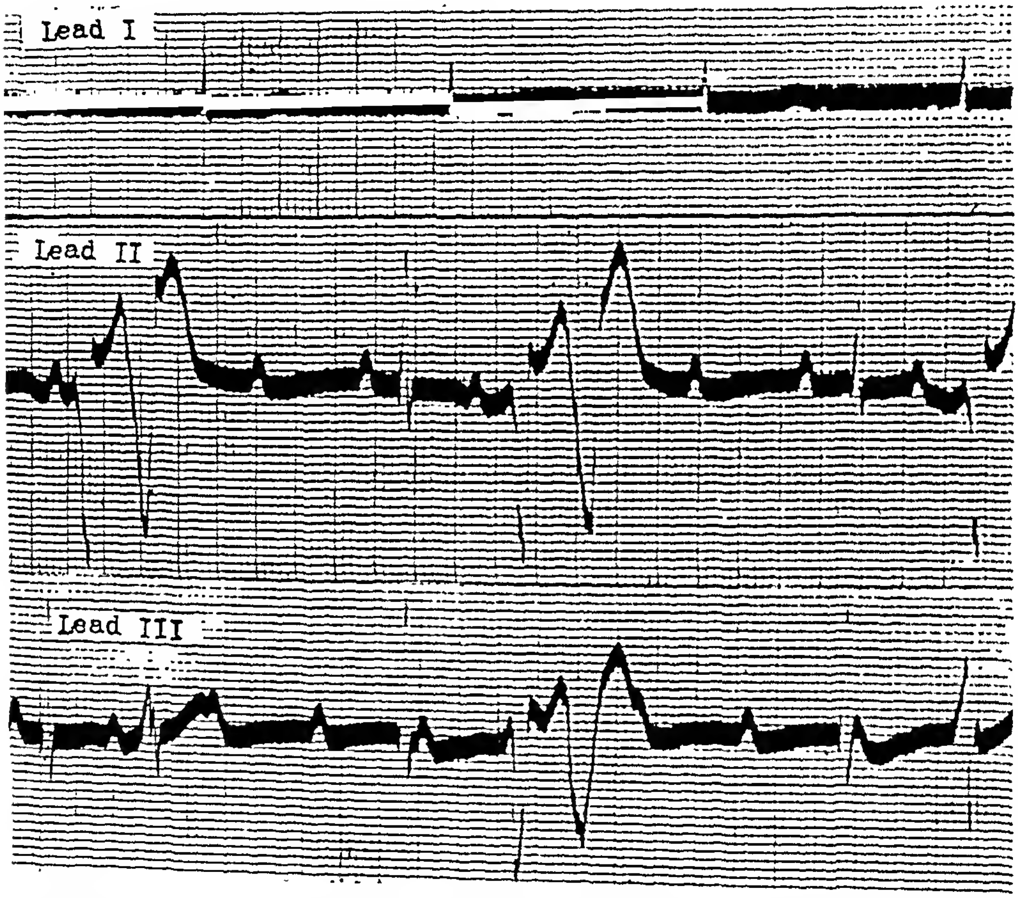

Fig. 3.—Case 1. Ecg. No. 3592. April 17, 1928, 5 P. M. Complete heart-block. Ventricular rate 48.4, Auricular rate 108.6. Bigeminal and trigeminal rhythm due to premature beats of ventricle.

breathing, and numerous moist râles. Because of the increase in respirations to 25 and the rise in temperature to 101.5° F., together with the physical signs, a diagnosis of bronchopneumonia was made. The ventricular rate, on this day, was never found to average more than 37 beats per minute when counted over long periods of time. At 11:50 A.M. of this day, the patient was given orally 6 c.c. of the tincture of digitalis. She received two more doses of the drug of 6 c.c. and 8 c.c. respectively within the next twelve hours, so that she received a total of 20 c.c. of the drug in a comparatively short time. Her condition was followed very closely and hourly heart rate and pulse readings were taken for the next seventy-two hours. These were checked by repeated electrocardiograms taken at various intervals during day and night. Despite the large doses of the drug, the patient

did not experience any nausea or vomiting. A definite increase of her ventricular rate independent of any premature beats was not noted until the following day.

April 17, 1928.—The general condition of the patient on this day was very poor. She was stuporous and in a semicomatose condition. The temperature was 102.3° F., the respirations were 26, and the pulse was intermittently regular and irregular but remarkably forceful. The signs of bronchopneumonia had spread to the opposite lung.

The electrocardiograms taken on the morning of this day showed a definite increase in the idioventricular rate which varied between 47.6 and 48.4, not counting the premature beats. The auricles now averaged 100 beats per minute. At times the heart rate would be regular for very long periods. At other times there were alternate premature beats of the ventricles, causing a bigeminal, trigeminal, and frequently quadrigeminal rhythm. Sometimes during the bigeminal periods, the alternate premature beats of the bigeminy would first assume the character of a

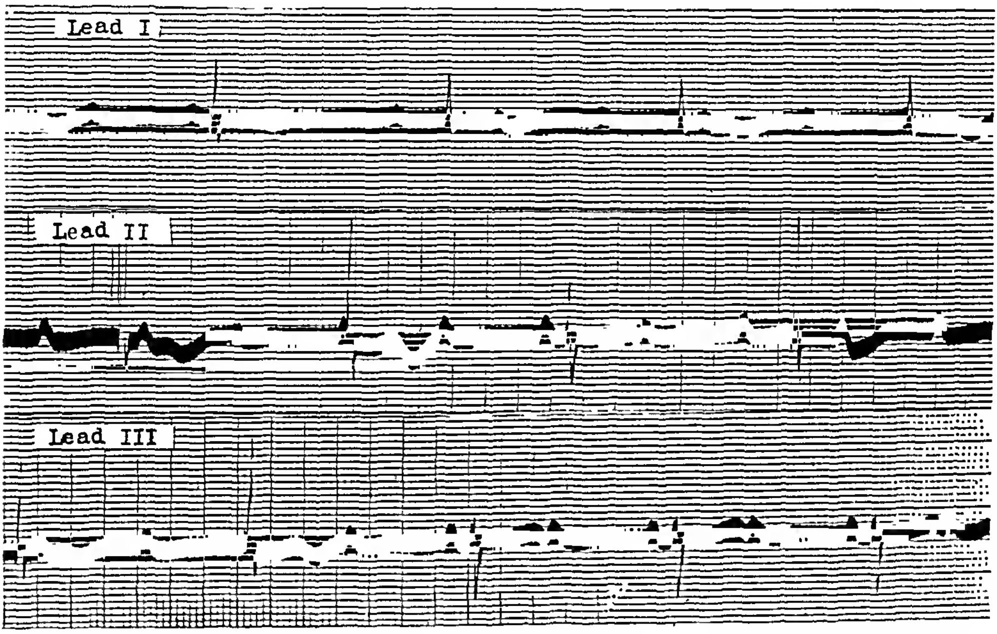

Fig. 4.—Case 1. Ecg. No. 3596. April 18, 1928, 11 A. M. Complete heart-block. The ventricular rate varies from lead to lead. It is 35.7 in Lead I, 43.4 in Lead II, and 42.8 in Lead III. Lead III shows an abrupt change from complete to partial heart-block which is accompanied by a transition from a dextrocardiogram to a levocardiogram. Note that the QRS group as well as the T-waves is affected by this change. The T-waves are now negative in all the leads showing complete heart-block.

dextrocardiogram and then suddenly change to a levocardiogram. The returning cycle following the premature beats of the bigeminy was always equal to the cycle of the idioventricular beat immediately preceding when the latter was not accompanied by an extrasystole. There were no changes in the size, shape, or form of the ventricular deflections at this time (Fig. 2).

Electrocardiograms taken between 2 and 5 P.M. of this day revealed no appreciable change in the ventricular rate from that noted above. The auricular beats, however, showed an increase to an average of 108.6 beats per minute. There were now to be noted definite variations in the initial ventricular deflections. These consisted in marked lowering of the voltage of the QRS group in Lead I and similar but slighter changes in Lead II. The T-wave was distinctly smaller in all three leads, with a tendency to negativity in the first lead. The P-wave was definitely increased in size. The predominating irregularity consisted of a bigeminal and

trigeminal rhythm due to premature ventricular beats some of which showed an abnormally wide deflection. At times there were long intervals when the ventricular rate was regular (Fig. 3).

April 18, 1928: On the morning of this day the patient appeared slightly better in that she was able to take some nourishment. The pulse rate was regular and very forceful. The average ventricular rate, counted over long periods of time, was 48 beats per minute. The electrocardiograms confirmed the absence of any irregularities until late in the day. Of particular interest in the records of this afternoon were the sudden and abrupt alterations in the form of the ventricular

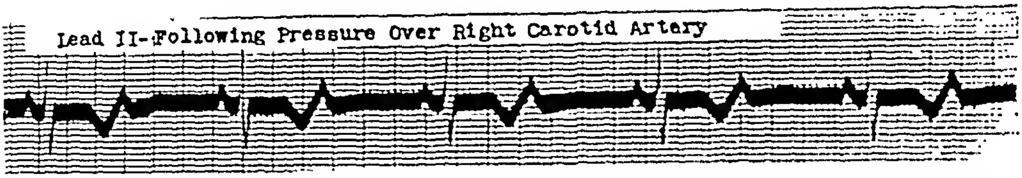

Fig. 5.—Case 1. Ecg. No. 3597. April 18, 1928. Lead II only. Partial heart-block, 2:1, following pressure over the right carotid artery. Note the slowing of both the auricular and the ventricular rates. The auricular rate has been reduced by this method from 100 beats per minute to 90.9 and the ventricular rate is now 45.4, whereas it was 48.2 before. Note that the T-wave is markedly negative now as compared with the single atypical complex of Lead II in Fig. 4.

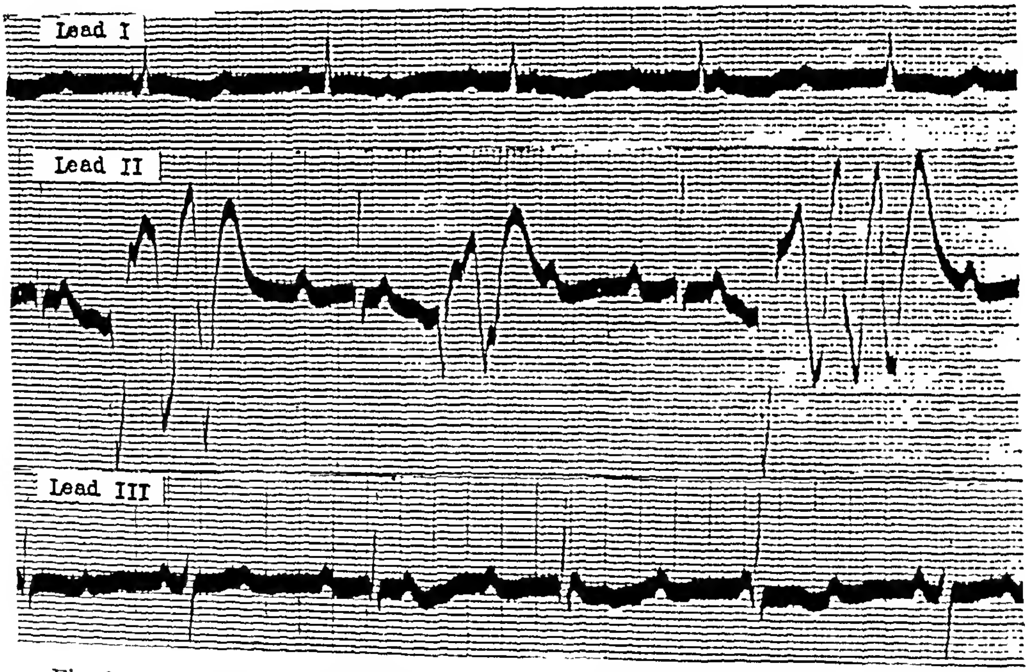

Fig. 6.—Case 1. Ecg. No. 3602. April 19, 1928. Complete heart-block. Basic ventricular rate is 53.5. Auricular rate is 125. Lead II shows premature beats of the ventricles arising from multiple foci, bringing the rate of the ventricles at such times as high as 300 beats per minute.

complexes of the electrocardiograms, which included the QRS groups as well as the T-waves. The QRS changed suddenly from a dextrocardiogram to a levocardiogram and the T-waves assumed a positive direction from a formerly negative one. When this took place there was a concomittant change from what was formerly a complete heart-block to what appears as a partial and incomplete 2:1 heart-block, with a sudden increase of the dominant idioventricular rate from 42.8 beats per minute to 48.2 beats per minute. When these abrupt variations in rate appeared in the electrocardiograms, the P-R interval always measured about 0.180 sec. They were present in all three leads, and it was particularly noticeable that the QRS as well

as the T portion of the ventricular complexes showed changes at the same time (Fig. 4). (It is to be noted that in some of the records of the previous day the change involved only the QRS complex, the T-wave remaining the same.)

Pressure over the left carotid sheath, at a time when the ventricular complexes did not show any of the variations described above, resulted in what appeared to be a change from a complete heart-block to that of partial 2:1 block with a decrease in the ventricular rate from 48.2 to 45.4 beats per minute and a slowing of the auricular rate from 99.3 to 90.9 beats per minute (Fig. 5).

April 19, 1928: The patient was now in coma, but the respirations were regular and 30 per minute. The temperature was 103.2° F., and the signs previously noted at the periphery of the lungs had now spread to the central part. The pulse was very forceful and again, as on the previous day, there were intermittent periods of regular and irregular rhythm. The ventricular rate of the dominant idioventricular rhythm was now 53.5 beats per minute and the auricular beats averaged 125. It was difficult at times to make out the arrhythmia of the heart clinically,

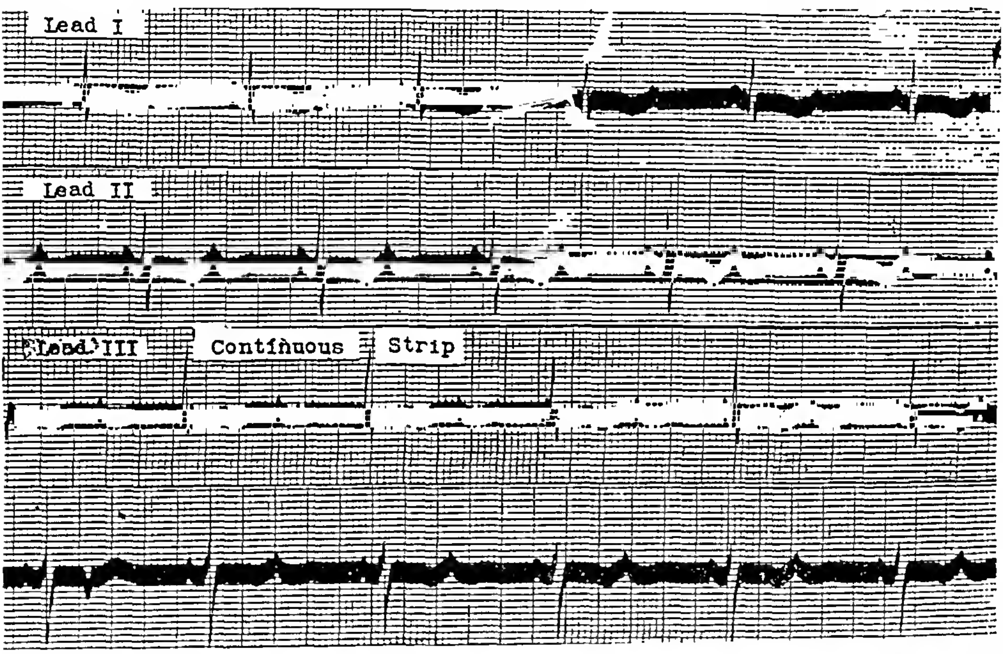

Fig. 7.—Case 1. Ecg. 3604. April 20, 1928, 1 A. M. Partial heart-block, 2:1. Lead III shows transition from complete to partial heart-block. Ventricular rate is 54.8, the auricular rate is 115.3. Note the change in rate with transition of complete heart-block to transient heart-block. The rhythm is now regular.

but the electrocardiograms revealed frequently innumerable premature beats of the ventricles with complexes of extremely wide deflections following the normal beats in groups of from 3 to 5 beats at a time. The impulses appear to be arising from several foci at the same time and are superimposed upon each other. Their presence brings the rate of the ventricles as high as 250 beats per minute. Changes in the ventricular deflection are still present, and they appear as abruptly as in other records but are especially noticeable in Lead III. Again it is to be noted that a sudden transition from a dextrocardiogram to a levocardiogram invariably takes place only at a time when the P-R interval measures a certain length, now approximately 0.160 sec. or 0.180 sec. In these records both the QRS and the T-waves are changed at the same time, that is, when the QRS complex assumes the form of a levocardiogram, the T-wave becomes positive (Fig. 6).

April 20, 1928: The patient was distinctly worse this morning. She was now totally unconscious and incontinent of feces and urine. The temperature was

103.4° F., the respirations were 30, and the pulse rate was 60 and almost perfectly regular. There were no premature beats to be heard at all. The interesting feature of the electrocardiograms on this day was the alternate periods of intermittent partial and complete heart-block. The transition from complete heart-block to partial heart-block (2:1) was associated with an abrupt change of the initial ventricular deflections from a dextrocardiogram to a levocardiogram and increase in the ventricular rate from 53.5 to 60 beats per minute. There were no coincident changes appreciable in the auricular beats which now averaged 93.7 beats per minute (Fig. 7).

April 21, 1928: On the morning of this day pulmonary edema set in. The temperature and respirations were about the same as on the previous day. The pulse was very forceful and regular. The ventricular rate averaged 65.2 beats per minute, and the auricular rate was now at its highest level of 125 beats (Fig. 8). The electrocardiograms showed complete aurieuloventricular dissociation with complete heart-block. The T-waves were negative in all three leads. The highest rate recorded was 71 beats per minute, when the ventricular rhythm was known

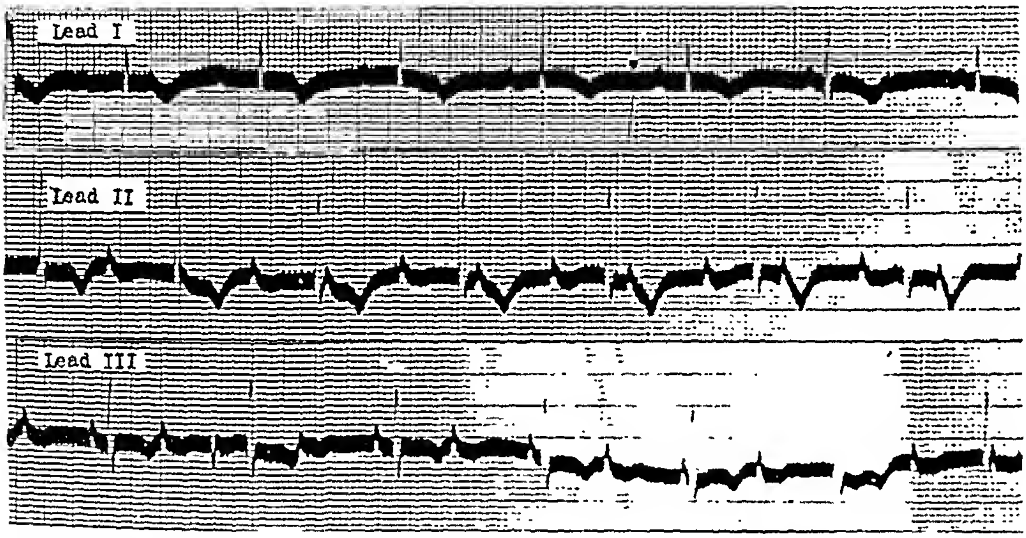

Fig. 8.—Case i. Ecg. No. 3607. April 21, 1928, 10 A. M. Complete heart-block. Ventricular rate is 65.2. Auricular rate is 125. The rhythm is regular. The T-waves are all markedly negative, showing the patient to be deeply under the influence of digitalis. Compare with Fig. 1.

to be regular. The rate kept up at about that level until 6 P.M. of this day when, because of the patient's general condition, observations had to be discontinued. She died on the evening of this day.

Comment.—In this patient a therapeutic dose of digitalis administered within twelve hours produced a slowing of the auricular rate from 99 beats to 78 beats per minute but did not accelerate the ventricles. Three weeks later, after the effects of the drug had worn off as judged by the return to normal of the auricular rate and the T-waves of the electrocardiogram, the patient was given orally approximately one and a half times the first dose of digitalis within twelve hours. One day following the administration of this amount of the drug, the dominant ventricular rate showed a sudden increase from 37.3 to 48.4 beats per minute. From then on the increase in the idioventricular rate was progressive until it reached 65.2 beats per

minute one day prior to death, independently of the presence of any premature beats. The auricular rate showed a similar progressive increase until it averaged 125 beats per minute, the highest figures recorded in the electrocardiograms.

The possibility must be considered that the bronchopneumonia was responsible for the increase in the ventricular rate. While it is well known that fever increases the heart rate of patients with normal sinus rhythm, in complete heart-block observations on this point are lacking. In one patient with lobar pneumonia who did not receive any digitalis, who was followed at the Montefiore Hospital, the rise in temperature due to the lung infection did not influence the rate of the ventricles. It would seem probable that in complete heart-block due to organic involvement of the bundle of His, the factor of pyrexia may be discounted as responsible for increasing the ventricular rate.

Again it may be questioned whether a uniform rise in the dominant ventricular rate might not have been an ante-mortem acceleration as has been observed by De Graaf and Wise in one of their patients with complete heart-block. The presence of simultaneous irregularities in rhythm in the electrocardiograms, such as multiple premature beats and the inversion of the T-wave, which became more prominent in all three leads from day to day, lend weight to the view, however, that both the increase in rate and the disturbances in rhythm are due to one and the same factor, namely, excessive digitalis administration.

CASE 2.—M. L. L., aged sixty-nine years, a peddler, was first seen on November 4, 1925. He had been in good health up to one year before (June, 1924) when he first began to complain of shortness of breath, progressive swelling of the lower extremities, and paroxysmal precordial pain, especially at night. He also suffered from pain over the right upper quadrant. Although at the beginning of his illness he could attend to his work, in the last six months he had been confined to bed because of weakness and swelling of the abdomen and scrotum.

Physical examination at this time (November 4, 1925) revealed an old, cyanotic man whose breathing was labored and of the asthmatic type, with prolonged wheezing expirations. There was cyanosis of the lips, cheeks, and finger nails. The superficial vessels of the neck were markedly distended and showed definite visible pulsations. The chest was moderately barrel-shaped.

The heart was markedly enlarged, the left lower border reaching the sixth intercostal space in the anterior axillary line. The heart sounds were of fair quality. A loud blowing systolic murmur replaced the entire first sound at the apex. The aortic second sound was accentuated. In the long diastolic silences, two and sometimes three muffled sounds could be heard best at the third intercostal space to the left of the sternum. These sounds corresponded with the systolic pulsations in the superficial veins of the neck, which were seen in the absence of a corresponding apical beat. The pulses were equal in force and time and were Corrigan in type. The rate was only 32 beats per minute. The radial arteries were tortuous, beaded, and rigid. The blood pressure varied between 300/80 and 210/80 mm. There was marked dullness over both lungs posteriorly. On the right side breathing was diminished from the angle of the scapula to the base. The abdomen was distended and there was shifting dullness. The liver was enlarged to 20 cm. below the costal margin. It was painful and tender to touch, but it was not pulsating. The

scrotum was markedly edematous and enlarged to the size of a grapefruit. The thighs and legs were extremely swollen. The prostate was large and nodular.

Course and Progress.—On daily doses of 3 c.c. of the tincture of digitalis orally for a period of twenty days, the edema of the scrotum and extremities cleared up completely, the ascites disappeared, but the fluid in the chest had to be removed by thoracentesis. In three months' time his weight came down from 194 pounds to 136. He was able to be up and about and no longer had to be restricted in his fluids. The liver, however, did not recede and remained practically the same throughout the rest of his life.

On April 14, 1926, the patient began to show symptoms of prostatic obstruction. He could not void, and on several occasions had to be catheterized. Shortly after the onset of these symptoms, he again began to experience shortness of breath. In two days' time, there was definite evidence of fluid in the right chest and swelling of the legs. An electrocardiogram taken at this time revealed the presence of complete heart-block with a ventricular rate of 88. Because of the increasing symptoms of heart failure, the patient was admitted to the wards of the Montefiore Hospital.

On April 23, 1926, he was given orally 10 c.c. of the tincture of digitalis, and

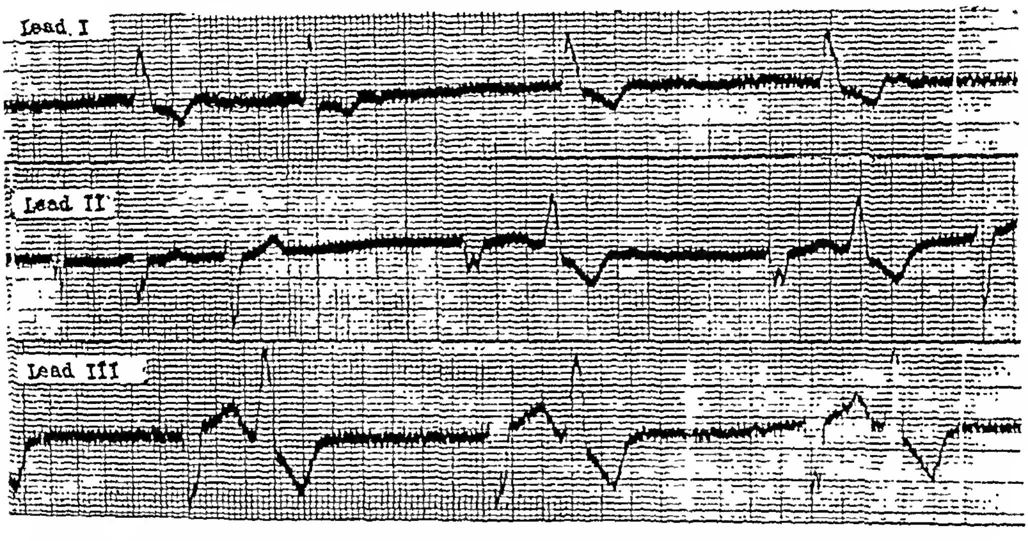

Fig. 9.—Case 2. Ecg. 1837. May 3, 1926. Complete heart-block. Auricular fibrillation. Premature beats of ventricle singly and in groups. In Lead II they are interpolated at both ends of the record.

this was followed within the subsequent three days by 10 c.c. more, so that he received a total of 20 c.c. of digitalis in three days. Two days after he received his last dose there was very marked increase in the heart rate, which became slightly irregular and averaged about 56 beats per minute. It was noted at the same time that the superficial jugular veins no longer showed the regular pulsations seen on previous occasions when his heart rate was regular. Clinically it was very difficult to distinguish the irregularity present. An electrocardiogram revealed complete heart-block, auricular fibrillation, and premature ventricular beats both isolated and in groups, many of which were interpolated (Fig. 9). At times these formed a bigeminal and trigeminal rhythm, but there was no definite sequence in their appearance. With the onset of these abnormal rhythms, the patient experienced fainting sensations and periods of momentary loss of consciousness. He complained that every other minute everything got "black" before his eyes.

All medication was discontinued except the usual sedatives. One week later all ventricular premature beats had disappeared, but the auricular fibrillation persisted. It was not until a little over six weeks after the onset of these arrhythmias that restoration to the normal basic rhythm of complete heart-block was observed. Clin-

ical examination at the time, June 6, 1926, revealed a regular ventricular rate of 32 beats per minute. In the long interventricular silences, there were two definite jugular pulsations accompanying two weak heart sounds now best heard at the level of the fourth intercostal space to the left of the sternum. The lungs were clear; the liver, however, remained enlarged as previously. There was no edema of the legs.

The patient remained in fairly good condition for several months after this episode, but at no other time was fibrillation of his auricles noted either clinically or graphically. He died suddenly while sitting in a chair on September 24 of this year.

Comment.—The dominant idioventricular rate of this patient was not influenced at all during the administration of daily doses of 3 c.c. of the tincture of digitalis over a period of twenty-one days, although the general condition and symptoms improved remarkably during that time. As a matter of fact careful measurements of the electrocardiogram revealed that at the time he received his first course of digitalis, from which he benefited considerably, the ventricular rate was even slower than at any subsequent observation. The ventricular rate showed an appreciable increase only after the administration of large doses of digitalis within a comparatively short time. The increase was due primarily to the interpolation of premature beats of the ventricle arising in multiple foci. The dominant rhythm was completely disrupted by these when they appeared in groups, since many of them showed no definite sequence in their appearance. That the auricular fibrillation and the multiple premature beats were due to excessive digitalis action is suggested by the fact that the withdrawal of the drug resulted in the restoration of the dominant rhythm of complete heart-block.

The increase of the ventricular rate due to premature beats as a result of digitalis was a very undesirable effect in this patient because there were momentary periods of loss of consciousness at a time when the ventricular rate was a high as 107 beats per minute. On the other hand, his symptoms were best relieved by moderate doses of digitalis, and he remained free from edema and breathlessness as long as the drug was used in this manner. His death was probably due to acute coronary vessel closure and was not related to the administration of the drug. There was no increase in the ventricular rate shortly before his death.

Case 3.—L. R., man, aged fifty years, a tailor, was admitted to the Montefiore Hospital on August 5, 1927, and died on November 28, 1927. He had previously been observed at this hospital for a few days, leaving of his own accord to enter another institution.

The patient had been well and up and about until three years prior to admission (February, 1924), when he began to complain for the first time of difficulty in walking because of oppression in the epigastric region, which was worse on effort. Soon after, he became aware of breathlessness on exertion and noticed progressive swelling of his lower extremities during the daytime. Both of these symptoms

compelled him to seek medical attention in November, 1924, but it was not until one year later (November, 1925) that he entered a hospital. In the period of the next two years he was admitted to several institutions on nine separate occasions, besides being in constant touch with the out-patient clinics of four other hospitals from which we were able to obtain a consecutive story of his progress since the onset of his illness.

In the middle of the summer of 1925, the patient noticed that he could not walk a block in less than fifteen minutes because he had to stop every few steps to get his breath. At about the same time the swelling which was first limited to his feet progressed to his thighs and this increased his difficulty in getting around. Occasionally he would get nocturnal attacks of shortness of breath. In the next few months he observed that while at first the edema of the legs would disappear at night, toward the early part of November, 1925, the swelling persisted and was getting worse even though he remained in bed for the entire day. His first hospital admission was on November 10, 1925.

Physical examination at this time revealed an obese and well-preserved man who looked much younger than his age. He was sitting up in bed supported by several pillows, and breathing with difficulty. There was marked cyanosis of his lips and finger nails. The superficial veins of his neck were not distended. His chest was moderately barrel-shaped. The apical impulse of the heart was neither visible nor palpable and percussion of the cardiac outline was difficult because of the rounded contour of his chest. The heart sounds were of fair quality, the first sound at the apex being replaced by a soft blowing systolic murmur which could be heard all over the chest. The heart rate was 72 beats per minute, and there was an occasional premature beat with a compensatory pause. The pulses were of good quality. The radial vessels were slightly thickened and tortuous. The blood pressure was 144/90 mm. The lungs showed a moderate amount of moisture at both bases posteriorly. The abdomen was soft but large and lax. The liver edge could be felt 2 cm. below the costal margin. The spleen was not palpable. There was marked edema of the legs and thighs.

The Wassermann reaction was negative. The urea nitrogen was 21 mg. per 100 c.c. The urine did not show anything abnormal. An electrocardiogram taken at this time (November 11, 1925) revealed the presence of high grade intraventricular block. The QRS measured 0.160 sec. The P-R interval was prolonged to 0.280 sec. There was an occasional premature ventricular beat. Within the next few days there was a spontaneous increase of the P-R interval to 0.320 sec. with partial A-V block and dropped beats. Because of the presence of these signs, it was not deemed advisable at this time to give the patient any digitalis. His edema cleared up with rest in bed, restriction of fluids, and diuretics, so that he was able to leave the hospital in fairly good condition one month after his first admission. At the time of his discharge he was able to walk around very comfortably but slowly.

In the next few months, the patient attended an out-patient clinic but because of increasing discomfort from traveling to the clinic, he resorted to a local physician, who promptly placed him on graded doses of digitalis. (The dose is not known.) On his second admission to the hospital (September 24, 1926) the patient showed marked ascites and hydrothorax, both of which required immediate relief. He was very uncomfortable, his liver was now 5 cm. below the costal margin, and he showed marked edema of the legs. He was given no further medication except the usual sedatives for the night. Several electrocardiograms taken during the two months following his second admission revealed the presence of heart-block with a ventricular rate that varied between 40 and 44 beats per minute. At first the block was incomplete and showed a PR interval of 0.20 sec., with marked negativity of the T-wave in Leads I and II. It finally became complete and remained so until December, 1926, when there was a severe release of the block to an incomplete

one with 2:1 rhythm. The development of the complete heart-block was attributed to excessive digitalis therapy which the patient had received while at home. Nevertheless, between December 8, 1926, and January 13, 1927, the patient was again treated with digitalis because of the recurrent ascites and hydrothorax. In that period he received a total of 69.5 c.c. of the drug at the rate of 30 minims, at first only once a day and then at intervals several times a day. He did not develop complete heart-block again until January 28, 1927, but despite these arrhythmic variations he was feeling much better under the influence of the drug than without it.

Between this last date and his admission to the Montefiore Hospital he had to be admitted to the wards of several institutions because of dyspnea from excessive accumulation of fluid in his chest. From repeated electrocardiograms taken in this interval, it was noticed that his rhythm varied between a complete heart-block and an incomplete one depending upon whether or not he was under the influence of digitalis. As his illness progressed, it could definitely be seen, however, that he no

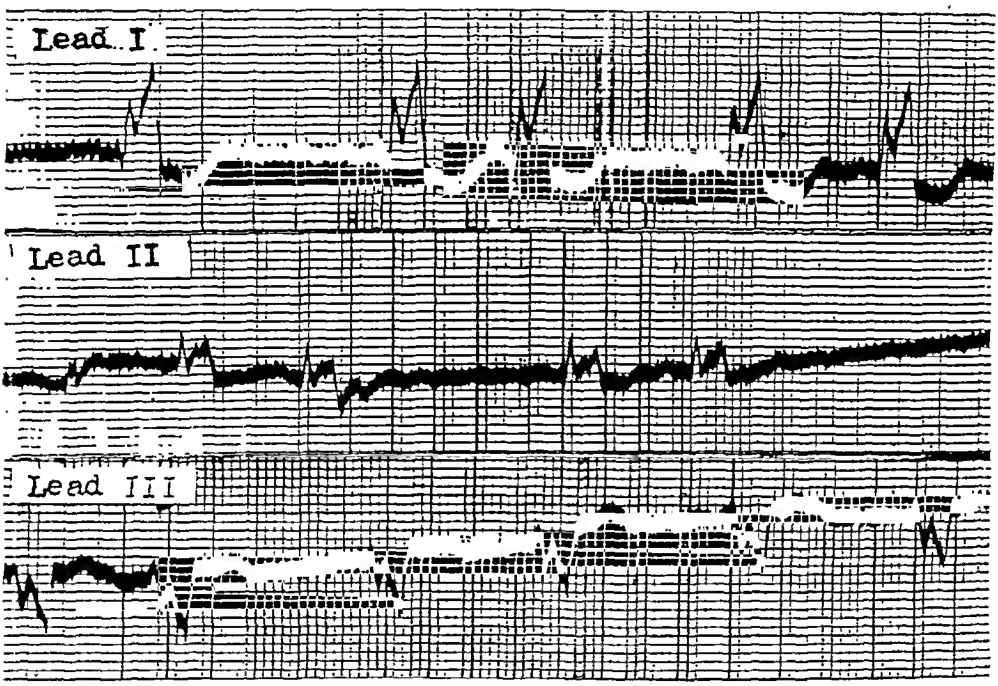

Fig. 10.—Case 3. Ecg. No. 2813. Aug. 9, 1927. Complete heart-block. Auricular fibrillation. Acceleration of the ventricular rate due to stimulation of the idioventricular pacemaker. Ventricular rate averages 87 beats per minute. Compare with following record.

longer responded to the drug as he had in the previous two years. Whereas, formerly his edema and breathlessness had become better with the use of digitalis, now, in the summer of 1927 he required more diuretics and abdominal taps for relief of symptoms. His ventricular rate during most of this time did not vary more than 8 beats per minute when he showed complete heart-block. Of unusual interest is the fact that premature beats were not observed in his latter records when it was well known that he was under the influence of digitalis.

In the ten days prior to his admission to the Montefiore Hospital he had received 2 c.c. of the tincture of digitalis once a day for the first three days and the same dose three times a day for the remaining seven days. Although when first seen in our wards, it was known that he had a complete heart-block with a ventricular rate of 40 and an auricular rate of 68 beats per minute, because of his very marked generalized anasarca, it was thought advisable to try further dig-

italis medication. His weight being 215 pounds, he was given 8 c.c. of the tincture of the drug on his admission. When seen two days later, he was so dyspneic that the only way in which he could find comfort was by sitting across the bed with his legs hanging over the side and his head bent over his chest. He was intensely cyanotic. His nose, lips, and ears were almost black. Because of the swelling of his face and neck, the superficial jugular veins were not visible. The apex impulse of the heart was neither visible nor palpable, and percussion of the cardiac outline was difficult because of the contour of his chest. The heart sounds were of poor quality, the first sound at the apex being replaced almost entirely by a loud systolic murmur which was heard best near the apical region. The heart rate was rapid and totally irregular. It varied from minute to minute and averaged 98 beats per minute when counted over a prolonged period of time. At times on auscultation there was definite bigeminal rhythm, and at other times there were groups of beats coming in pairs but irregularly spaced. At other times the irregularity had the rhythm of a definite quadrigeminy. The pulse was of good quality and forceful. There was no deficit. The lungs were remarkably free from moisture. The ab-

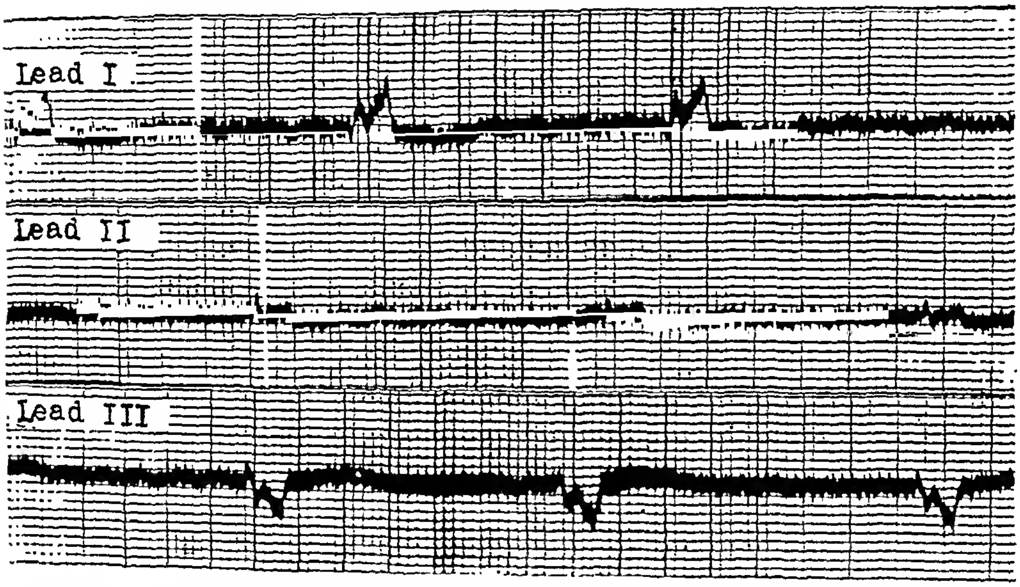

Fig. 11.—Case 3. Ecg. No. 2826. Aug. 24, 1927. Complete heart-block. Auricular fibrillation. Ventricular rate now averages 40 beats per minute. Note the disappearance of ventricular arrhythmia. The voltage of QRS is lower than in previous record.

domen was slightly swollen, and there was shifting dullness. The liver edge was down to the level of the umbilicus and the legs were extremely swollen.

An electrocardiogram taken at this time (Fig. 10) reveals a variable ventricular rate with a maximum of 93 beats per minute. The beats show a tendency to coupling. The QRS complexes are 0.20 sec. in duration and markedly notched. Their voltage is variable from lead to lead, the maximum being 12 mm. high in Lead I. There is no definite evidence of a P-wave to be seen in any of the leads. The ventricular complexes resemble one another very much from beat to beat so that it is impossible to state which is the dominant beat of the rhythm. Digitalis was discontinued, and the patient did not receive any more of this drug during the rest of his period of observation.

He was made comfortable with adequate opiates, and in the next few days he showed some improvement in that he was able to lie down comfortably and take nourishment. His chest and abdomen were tapped again within a week, but the edema of the legs persisted until the end. On August 24, 1927, the electrocardiogram showed very clearly a complete heart-block, with a ventricular rate varying between

38 and 42. The voltage of the QRS complexes was distinctly lower and there were no evidences of regular auricular activity which was now replaced by auricular fibrillation (Fig. 11).

On September 7, 1927 almost one month after his admission, the patient was looking and feeling slightly better. Although his legs were swollen, he was able to eat and sleep comfortably and even asked to be wheeled around in a chair for a while each day. On this day his rhythm was almost perfectly regular. His pulse rate was 40 and in the sitting position, with his head in slight dorsal extension, it was possible to see the jugular pulsations in the interventricular silences. The electrocardiogram (Fig. 12) confirmed the regularity of the heart-block and in addition revealed the presence of a regular auricular rate at an average of 88 beats per minute. The QRS complexes were distinctly lower than at any other previous examination.

The complete heart-block persisted with but very little variation in both the auricular and ventricular rate until he died from cardiac failure on November 27, 1927. On the day of his death, the ventricular rate fell to about 10 beats per minute shortly before he expired.

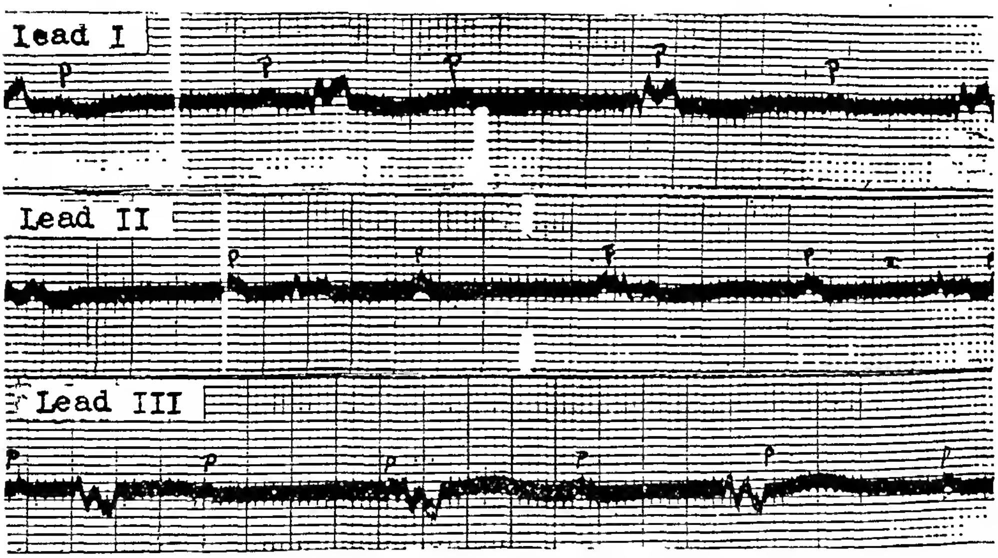

Fig. 12.—Case 3. Ecg. 2844. Sept. 7, 1927. Complete heart-block. Ventricular rate 40. Auricular rate 88. Note the auricles are regular now. Compare with previous record.

Comment.—This patient with marked myocardial involvement was followed over a period of two years. In the early stages of his illness he showed various degrees of block, but changes from one form of block to another were never accompanied by any Stokes-Adams seizures. A stage was reached in his illness when the block became permanent, and he no longer responded effectively to any form of medication. Despite the variable changes in rhythm that he exhibited from partial to complete heart-block, the patient benefited considerably from the administration of digitalis for over one and a half years after he began to show signs of heart failure with decompensation. At no time after the establishment of complete heart-block was there noted any increase in the ventricular rate except after he had received digitalis in excess of the usual doses to which he had been accustomed.

After the administration of 50 c.c. of the drug within eight days, he developed an irregular acceleration of the ventricles with auricular fibrillation. The ventricular irregularity disappeared within a few days, but the fibrillation persisted for several weeks.

DISCUSSION

An appreciation of the effects of any drug on the automatic beating ventricles in human beings must first take into account the inherent variability of the ventricles in complete heart-block as seen from day to day over a prolonged period of time. In summarizing such changes, Frey[13] has called particular attention to the fact that many patients with complete heart-block exhibit spontaneous premature beats in the slow interventricular periods. Usually there is no compensatory pause following these. Sometimes the premature beats are interpolated, but compensatory pauses may be present. Infrequently, a complete ventricular cycle may drop out with perfect regularity. The dominant beats of the ventricles may not be disturbed by such omissions. Furthermore, there may be periodic reductions and increases in the frequency of the idioventricular contractions so that they seem to resemble Luciani periods. These are seen particularly in patients subject to Stokes-Adams syndrome. For such reasons any study of the effects of digitalis on the rate of the ventricles in complete heart-block must be correlated with the antecedent rate and rhythm which the patient presents before the drug is used. Obviously if the patient's rate is very labile and varies from day to day, that amount of variability must be taken into consideration in judging the results produced by an effective dose of digitalis.

In the three patients reported in this paper, the dominant ventricular rate as counted over a prolonged period of several months during the presence of heart-block, never varied more than 10 beats per minute at any period. In all of the 3 patients spontaneous premature beats were recorded at some time during the course of their illness. In 1 case a single body-weight dose of digitalis caused the premature beats to disappear. In 2 patients the administration of a larger dose of digitalis than a body-weight measure resulted, however, in the production of numerous premature beats of the ventricle arising from multiple foci. In the first case all of these disappeared as the dominant ventricular rate increased from the toxic action of the drug. This is consistent with experimental findings where it is constantly observed that premature beats of the ventricle disappear when the ventricles themselves take on a higher rate than the inherent basic rate.

In this respect it is important to note how closely the appearance of the abnormal rate and rhythm in man may be compared with similar disturbances in animals, following the use of toxic doses of digitalis after the establishment of complete heart-block. For example, von

Egmond[14] has tabulated from his researches and from those of others a definite sequence of events following the absorption of digitalis in complete heart-block. In the first stage, there are no irregularities. The idioventricular rhythm remains the same and it is slow. A second stage follows which is characterized by the appearance of premature beats in a dominant ventricular rhythm of relatively low rate. The frequency of the ventricles may then increase suddenly to a very high rate which may be at first either regular or irregular, depending upon the amount of drug used.

The auricles may also beat fast, or if the vagus is influenced by the drug they may beat slowly, but this is characteristic of the first stage only. The slowing of the auricles is frequently followed at such times by a change from complete heart-block to what appears as a partial 2:1 heart-block or even a normal rhythm.[12] But in man the features of an incomplete heart-block with 2:1 rhythm have been considered hitherto only apparent and the consequence of a fortuitous change of the auricular to the ventricular rate under the slowing of digitalis on the auricles.[17]

In 1 of our patients, however (Case 1) the change from complete heart-block to partial heart-block is not apparent but real, since the P-R interval preceeding the QRS complexes in the records showing partial heart-block are equal from beat to beat. Besides in this patient during the stages of complete heart-block, pressure over the carotid artery in the neck resulted in no changes whatsoever in either the ventricular rate or rhythm, whereas during the appearance of the partial heart-block both the auricles and ventricles were slowed by carotid pressure. The explanation for this unusual phenomenon is not clear.

Nevertheless, an appreciation of these sudden changes in rate and rhythm during the administration of digitalis and the initiation of the abrupt forms of the ventricular tachycardias cannot be overestimated in man, for they may be the first index of overdigitalization in patients with complete heart-block who are receiving the drug.

A study of the electrocardiograms accompanying this report reveals that the increase in the ventricular rate in already established complete heart-block as a result of digitalis may be one of several types.

1. There may be a progressive uniform increase in the dominant rate of the ventricles *independent of* the *presence of* any premature beats.

2. A further increase in the rate after it has already been augmented by digitalis may take place by a sudden change from complete heart-block to partial heart-block. Such a transition may be seen in the records of Case 1, where the change in rate is also accompanied by a change in rhythm when a complete heart-block becomes a partial heart-block.

3. An increase of the ventricular rate may also occur from the stimulation of multiple ventricular foci, giving rise to premature beats. These may be single or in groups, forming a bigeminal, trigeminal, or quadrigeminal rhythm. In some instances the beats are interpolated while in others they may be superimposed on each other so as to bring the rate as high as 300 beats per minute at times. It is probable that ventricular fibrillation is the next step, although fortunately it has not been observed in our studies.

DIGITALIS AND THE DEVELOPMENT OF TRANSIENT AURICULAR FIBRILLATION IN COMPLETE HEART-BLOCK

Transient auricular fibrillation was observed as a toxic manifestation of digitalis administration in 2 patients with complete heart-block. In both patients the arrhythmia set in suddenly and without the electrocardiographic evidence, recognition would have been impossible. In one patient, the auricular irregularity was masked by the presence of premature beats, most of which were interpolated in groups (Case 2). These disappeared after three days, the polygeminal rhythm giving way to a trigeminal then to a bigeminal rhythm and finally to isolated premature ventricular beats and then to the dominant idioventricular rhythm. The sequence of events in the other patient was somewhat similar, but the ventricular irregularity was due to stimulation of the idioventricular pacemaker rather than to multiple premature beats of the ventricle (Case 3). The auricles continued to fibrillate, however, in both cases for approximately four and six weeks respectively. In the first patient, the intravenous administration of atropine sulphate, gr. 1/100, on the fourth day after the establishment of auricular fibrillation did not produce any changes in either rate or rhythm for one-half hour, during which time electrocardiograms were taken every five minutes. There were definite changes, however, in the initial deflections of the ventricular complexes at the end of the experiment, a phenomenon which had been observed in this patient prior to the administration of atropine.

The auricular rate was greater in both patients following the disappearance of the fibrillation than it was before its onset. For example, in Case 2, the rate was 66 before and 82 after, whereas in Case 3, the rate was 69.3 before and 88 after. It seems evident that in both cases digitalis was able to cause slowing of the auricular rate through vagal inhibition shortly before the appearance of auricular fibrillation.

That auricular fibrillation might be a toxic manifestation of digitalis in complete heart-block has been suspected by previous observers. In a patient with complete heart-block who had been receiving digitalis, Hewlett and Barringer[9] noted the disappearance of

the "a" wave from the jugular tracing and at first regarded the incident as a defect in technic, but the second disappearance from the apical tracing during a second course of the drug suggested to them that this may have been due to a "toxic weakening of auricular contractions." The presence of an extrasystole on each occasion also suggested to them a toxic digitalis effect. Similarly Neuhoff[20] studied graphically a patient with complete heart-block with a rhythmic ventricular rate of 35 and an auricular speed of 32 beats per minute, as demonstrated by polygraphic and electrocardiographic tracings. Through inadvertence on the part of the nurse, digitalis was administered for several weeks, after having been ordered discontinued. The pulse then became arrhythmic. The auricular beats were no longer heard in the interventricular silences and extrasystoles, most of which were frustrated, were audible at the apex. Regular recurrent auricular waves could not be identified in the jugular tracings. Two weeks after digitalis was discontinued, heart-block was again present as shown by the electrocardiogram, and the auricular sounds could be heard again. From the auscultatory evidence, from the absence of the auricular waves in the jugular tracing, and from the fact that digitalis poisoning sometimes induces auricular fibrillation and extrasystoles, it seemed probable to him that the polygraphic tracings represented heart-block, auricular fibrillation and ectopic beats, "a unique instance of digitalis poisoning in a patient with complete heart-block."

In complete heart-block, the sudden simultaneous appearance of auricular fibrillation and premature beats, whether singly or in groups, during the administration of digitalis may be considered sufficient evidence that the onset of the irregularities was initiated by the drug.[21] The abruptness with which these rhythms set in without any premonitory signs or symptoms, such as nausea and vomiting, or isolated premature beats, is by no means rare in certain patients with normal sinus rhythm.[22] There is no reason why it should not be seen in patients with complete heart-block. The important fact to remember is that the onset of auricular fibrillation is a sign of excessive digitalization or digitalis hypersusceptibility, and it is to be used as an indication for the withdrawal of the drug. Very recently the possibility has been suggested[23] that these patients really present auricular standstill, as it is observed experimentally in animals when too much of the drug is introduced rapidly intravenously. In human beings this is an exceedingly rare phenomenon, and even though the electrocardiograms show no evidence of regular auricular activity, there are other criteria that must be considered before making a diagnosis of complete standstill of the auricles.[24]

CONCLUSIONS

1. Digitalis in therapeutic doses may be of great benefit to patients with complete heart-block and heart failure. The improvement in these patients takes place through the direct action of digitalis on the heart muscle and not through an acceleration of the automatic beating ventricles.

2. In 3 out of 8 patients with complete heart-block studied at the Montefiore Hospital, the ventricular rate was increased appreciably only after the administration of digitalis in doses larger than those commonly employed in therapeutics.

3. The increase of the ventricular rate in complete heart-block during the administration of digitalis is a toxic manifestation of the drug, and because of the undesirable effects calls for its immediate withdrawal.

4. Transient auricular fibrillation is another manifestation of digitalis intoxication in complete heart-block.

5. Since it is difficult to appreciate the various types of toxic rhythms that manifest themselves in complete heart-block during digitalis therapy, it is advisable to prescribe the drug to such patients, under careful graphic control.

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THE INCIDENCE AND SIGNIFICANCE OF ELECTROCARDIOGRAMS SHOWING THE FEATURES OF LEFT AXIS DEVIATION AND QRS OF NORMAL DURATION WITH INVERTED T_1 AND UPRIGHT T_3*

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CLINICAL evaluation of heart disease centers more and more around the question of the integrity of the myocardium. In like manner the value of the electrocardiogram has come to depend chiefly upon the amount of information it gives on this question. In the application of electrocardiography to the diagnosis of heart disease, therefore, chief interest at present attaches to the form of the ventricular complex. Full understanding of all components of the ventricular complex, however, has not been reached, and as a consequence of this incompleteness, clinical interpretation of certain abnormalities is still somewhat equivocal.

The factors which cause the electrical axis to deviate to the right or to the left, and thus determine the direction of the QRS complex are fairly well understood and are applied clinically with a certain measure of exactness. But much uncertainty exists with regard to the T-wave. Clinical interpretation of changes in its form and direction, therefore, is still attended with considerable difficulty. Willius[1] and others have shown that inversion of the T-wave (except in Lead III) carries an unfavorable prognosis, and it has become customary to regard records which show such inversion as indicative of "myocarditis" (or drug effect). Little is known, however, of the exact pathological processes responsible for the inversion. Notwithstanding this uncertainty, or perhaps because of it, there has arisen a tendency to consider separately the T-wave and the QRS complex rather than to study both in their relationship to each other. It may well be questioned whether this separate consideration of the initial and final phases of the ventricular complex has not impeded progress in reaching an understanding of it, particularly so far as the T-wave is concerned.

As a consequence of this separate consideration of the components of the ventricular complex, and of the relatively more complete knowledge of the initial phase, it has been customary to diagnose records showing the QRS complex upright in Lead I and downwardly deflected in Lead III, with QRS of normal duration, as "left ventricular predominance" or "left ventricular preponderance," no matter what may

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be the direction of the T-waves in either the first or the third leads of such electrocardiograms.

Various combinations of the initial (QRS complex) and final (T-wave) phases of the ventricular complex in such records are shown in Fig. 1. Each record in this figure indicates deviation of the electrical axis to the left. The fourth is an example of the type with which our paper deals. Other examples of this type are shown in Fig. 2.

There is much evidence that electrocardiograms of this particular type result from defective conductivity in the right limb of the A-V bundle rather than from other causes of left axis deviation. This evidence rests on both experimental and clinical data. Wilson and Herrmann,[2] by producing levogram and dextrogram independently of each other, obtained various records showing the results of superimposing one on the other with different time relationships. When levogram and dextrogram were superimposed synchronously, the resulting record, of course, had the form of the normal bicardiogram. But when the levogram was caused to anticipate the dextrogram, the resulting bicardiogram exhibited not a haphazard relationship of T-wave to QRS complex, but showed the precise relationship exhibited in the records which constitute the theme of our paper. Under the conditions of the experiment there was relative delay of conduction to the right side of the heart.

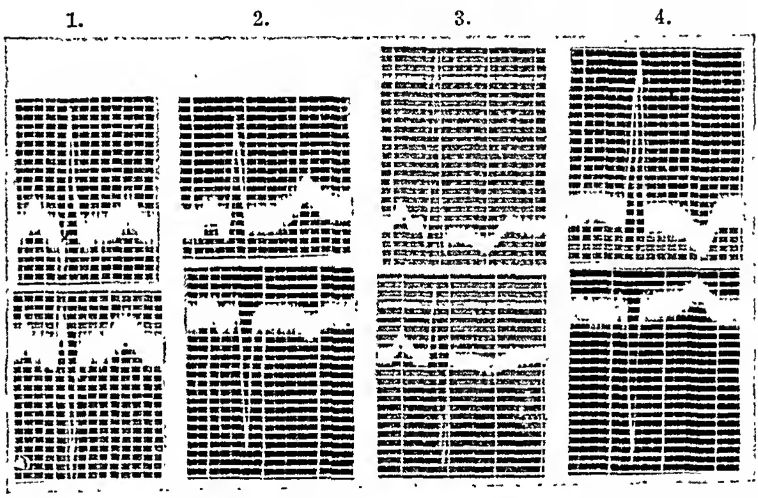

Fig. 1.—Electrocardiograms showing left axis deviation. In No. 4 the relationship of the T-wave to the QRS complex is that of defective conductivity in the right bundle-branch. In all figures Leads I and III are shown.

Clinical data also support the conception that these records represent defective conductivity in the right branch of the bundle. Such evidence is presented in Fig. 3. This shows four electrocardiograms of the same patient. They were made on August 14, August 19, August 24, and September 8, 1923, respectively. The first and second records in this figure show right bundle-branch block. The third and fourth conform to the type under discussion. In view of the recent complete

block in the right limb of the A-V bundle, it would appear more reasonable to interpret the later records in this case as representing defective conductivity in the right limb of the bundle than to ascribe their shape to some other cause of left axis deviation. Such an interpreta-

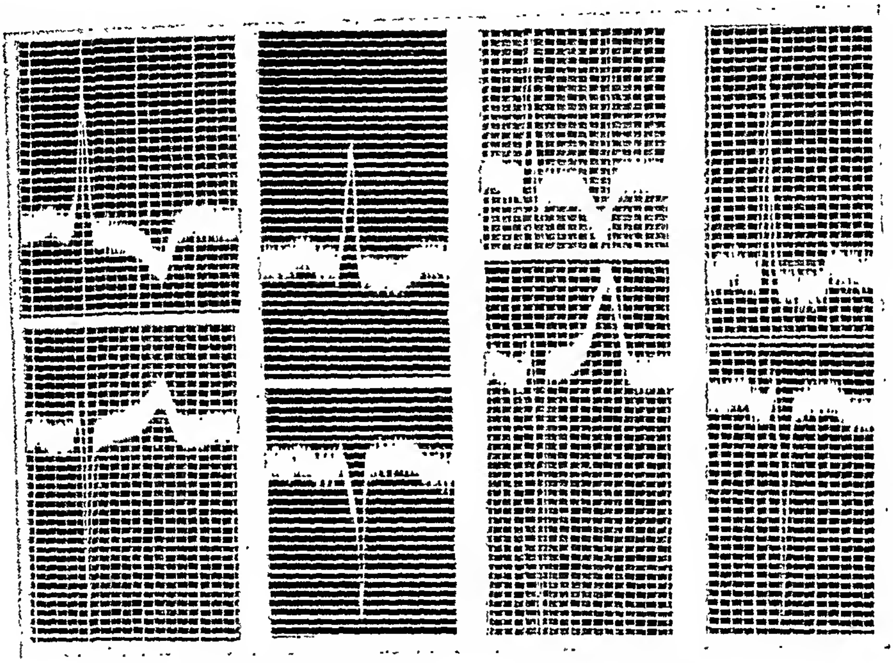

Fig. 2.—Additional electrocardiograms of the same type as No. 4 in Fig. 1.

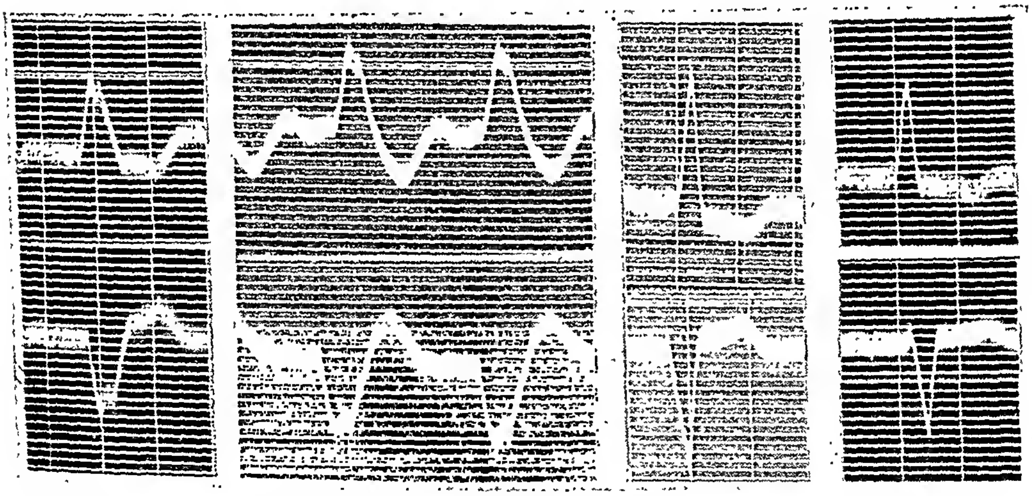

Fig. 3.—Four electrocardiograms from the same patient. The first was made August 14, 1923; the second, August 19, 1923; the third, August 24, 1923, and the fourth, September 8, 1923. The first two are indicative of right bundle-branch block. Note that the relationship of the T-wave to the QRS complex is the same in all four records.

tion is the only one which *alone* accounts for both the left axis deviation and the direction of the T-waves.

If impaired conductivity in the right branch of the A-V bundle, rather than relative left ventricular hypertrophy or other cause of left axis deviation, is the correct interpretation of the third and fourth

records in Fig. 3, the same interpretation may well apply to other such electrocardiograms obtained in cases in which right bundle-branch block has not previously been demonstrated. Records of this type and those showing right bundle-branch block may be expressions of the same process, which differs only in degree in the two instances. If so, the progress of heart disease in such a case might, on occasion, be followed electrocardiographically from the stage of delayed conduction in the right branch of the bundle to the stage of complete block in this branch. Electrocardiograms which give such a record of the progress of heart disease in a patient are shown in Fig. 4.

The patient in this case, a man fifty-four years old, had had hypertension for years. At the time of the first record, May 3, 1927, he had had few symptoms directly referable to his heart. In August, 1927, he

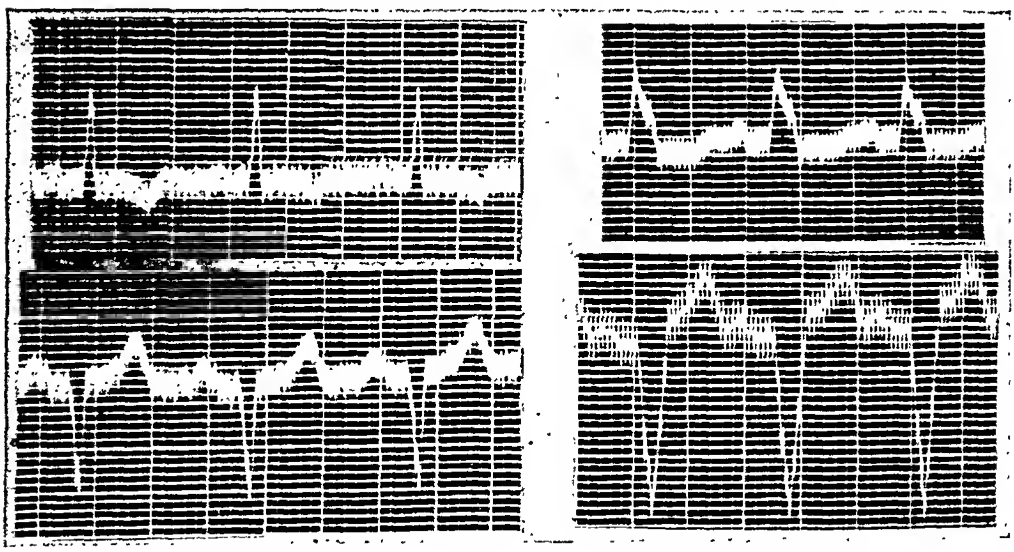

Fig. 4.—Two electrocardiograms from the same patient. The first record, made May 3, 1927, indicates defective conduction in the right bundle-branch. The second record, made October 25, 1927, shows right bundle-branch block. (Extraneous alternating current somewhat distorts the second record.)

had dyspnea, edema, and enlargement of the liver. The next record, October 25, 1927, shows right bundle-branch block. Subsequent records showed that the block persisted. This case offers additional clinical evidence that records conforming to the type described in the title represent impairment of conductivity in the right limb of the A-V bundle. It lends weight also to the suggestion just advanced that records of this type and those showing right bundle-branch block represent only different degrees of the same pathological process, and have, therefore, the same significance from the standpoint of etiological diagnosis.

The question whether these electrocardiograms do in fact represent defective right bundle-branch conduction is, of necessity, closely related to the question of etiology. What is the pathological process in

the bundle that is responsible for the impairment of conductivity? Is it the same in all, or at any rate in most, cases? An investigation of the significance of electrocardiograms of this type, therefore, involves two phases. First, an analysis should be made of all cases in which they occur in order to determine whether the cases present certain features in common. The results obtained from this study of incidence should then be applied to the question of impairment of conductivity. If certain features are indeed found to be constant, these should be investigated to see whether they might imply a conduction defect in the right limb of the A-V bundle.

It appeared to one of us that the incidence of these electrocardiograms is confined almost exclusively to cases of arteriosclerotic heart disease and hypertensive heart disease.* The primary object of our paper is to test the accuracy of that impression: to determine in fact, whatever their explanation, whether any common finding attends their incidence. The second object has been to apply the data thus acquired to the problem of defective conduction: to determine whether such data might indicate a pathological process of such character as to impair conductivity in the right branch of the A-V bundle.

METHOD OF STUDY

All electrocardiograms of the type described were withdrawn from our files. The criteria adhered to in the selection of records were the following: QRS deflection upright in Lead I, downwardly directed in Lead III; T-wave inverted or diphasic in Lead I, upright in Lead III; duration of QRS complex less than 0.10 second. The corresponding case histories were obtained and the following data noted: Age; sex; Wassermann reaction; highest systolic blood pressure; lowest diastolic blood pressure; all diagnoses both primary and secondary; whether or not there was a diagnosis of any cardiac abnormality; type of heart disease;† evidence of any degree of heart failure (past or present); evidence of cardiac enlargement; evidence of arterial sclerosis and condition of coronary arteries at autopsy.

RESULTS

There were 237 cases. The results are shown in Tables I, II and III. In 128 cases the electrocardiogram showed the T-wave completely inverted in Lead I, while in the remaining 109 cases the T-wave was more or less diphasic in the first lead.

*Such an incidence, if found to be correct, would at once associate them closely with records showing right bundle-branch block, and would lend still further evidence, therefore, to the conception that both result from the same pathological process.

†In the case of those histories which ante-dated the adoption of etiological classification in our files, the appropriate etiological diagnosis was supplied as well as possible from the data in the case history.

There were 150 males and 87 females. The age table shows the number of each sex that fall in each decade. The other tables are not subdivided on the basis of sex.

TABLE I

Showing the grouping of cases according to age and according to blood pressure.

AGE				BLOOD PRESSURE			
YEARS	NUMBER OF CASES MALE	FEMALE	BOTH	HIGHEST SYSTOLIC	NUMBER OF CASES	LOWEST DIASTOLIC	NUMBER OF CASES
Above 69	16	10	26	Above 249	22	Above 149	9
60-69	34	13	47	200-249	85	125-149	38
50-59	51	29	80	170-199	54	100-124	63
40-49	36	18	54	160-169	15	90- 99	31
30-39	10	13	23	150-159	16	80- 89	27
20-39	2	1	3	140-149	11	70- 79	18
Under 20	1	0	1	130-139	11	Under 70	39
No data	0	3	3	Under 130	14	No data	12
Total	150	87	237	No data	9		
				Total	237	Total	237

TABLE II

Showing the number of cases with and without: (a) arterial sclerosis, (b) cardiac diagnosis as principal diagnosis, (c) cardiac diagnosis as either principal or secondary diagnosis, (d) evidence of any degree of cardiac insufficiency, (e) any evidence of hypertrophy.

	ARTERIAL SCLEROSIS	WAS PRINCIPAL DIAGNOSIS A "CARDIAC DIAGNOSIS"?	DID DIAGNOSES (PRINCIPAL AND SECONDARY) INCLUDE A "CARDIAC DIAGNOSIS"?	WAS THERE EVIDENCE (PAST OR PRESENT) OF CARDIAC INSUFFICIENCY?	WAS THERE ANY EVIDENCE OF HYPERTROPHY?
Yes	163	97	132	131	207
No	47	137	102	100	23
No data	27	3	3	6	7

TABLE III

DIAGNOSIS 234

Showing division of cases into "Cardiac" and "No cardiac" groups, according to diagnoses on case history. The cardiac group is subdivided according to the type of heart disease. The non-cardiac group is subdivided according to whether or not a diagnosis of arterial sclerosis or hypertension appeared on the case history. Diagnoses in both groups above the dotted line carry more or less suspicion of coronary disease.

A CARDIAC 132			B NO CARDIAC 102	
Arteriosclerotic Hypertensive Angina	100	125	With: hypertension arterial sclerosis	96 (100)
Syphilitic Aneurysm	25			
Rheumatic Bac. endocarditis Thyroid	5 1 1	7	Without: hypertension arterial sclerosis	6 (2)

COMMENT

Age.—It will be observed at once that these electrocardiograms were found in people of middle age and beyond. Only 4 of the 234, whose ages were recorded, were under thirty years of age. Only 11 were less than thirty-five.

Blood Pressure.—These patients had hypertension. In 89 per cent of cases the systolic blood pressure at some time was recorded at least as high as 139 mm. In 70 per cent a reading at least as high as 170 mm. was recorded, while in 46.9 per cent a reading of 200 mm. or higher was found. The diastolic blood pressure was never recorded below 100 in 48 per cent of the cases. It was never below 80 in 74 per cent. The relatively large number with a diastolic pressure below 70 includes 25 patients with syphilis of the heart or aorta and two patients with rheumatic heart disease.

Arterial Sclerosis.—Arterial sclerosis was characteristic of these patients. In relatively few instances was an eyeground examination by a practiced ophthalmologist recorded, yet routine physical examination disclosed evidence of sclerosis in 78 per cent of the cases.

Cardiac Diagnosis.—In only 41 per cent of all cases was the principal diagnosis one relating to the heart or the aorta. Including all recorded diagnoses, both primary and secondary, a "cardiac diagnosis" occurred in only 132 cases (56 per cent).

Type of Heart Disease.—It is extremely interesting to note that of the 132 cases showing a cardiac diagnosis one hundred were cases of arteriosclerotic heart disease, hypertensive heart disease or angina pectoris; twenty-five were cases of syphilitic heart disease or aneurysm; while there were only five cases of rheumatic heart disease, one of thyroid heart disease, and one of bacterial endocarditis. In 125 of the 132 cases, then, there was more or less evidence (direct or implied) of some sort of coronary lesion.

Cases With no Cardiac Diagnosis.—Of the remaining 102 patients, those who had no cardiac diagnosis, there were only six in whose cases neither arterial sclerosis nor hypertension was diagnosed. In these six cases indeed no secondary diagnoses were recorded; the patients' ages ranged from forty-five to sixty-three years. The case histories gave evidence of sclerosis in three of the six cases; in another the blood pressure was 240/130 mm. The patients whose electrocardiograms are of the type under discussion and who give, at the same time, few clinical evidences of heart disease, have, then, almost without exception arterial sclerosis, hypertension or both.

Thus it will be seen that coronary disease or some disease which carries with it more or less suspicion of coronary involvement occurs almost without exception in the patients who presented electrocardio-

grams of this type. This is true whether examination gave enough evidence of heart disease to warrant a cardiac diagnosis or not.

Decompensation.—In 43 cases, or 18 per cent, there was a diagnosis of decompensation. Study of the histories indicated that some degree of cardiac insufficiency either had existed or was present in 88 of the remaining cases, thus bringing the total of those with past or present evidence of some degree of cardiac insufficiency to 131 cases (56 per cent).

Hypertrophy.—This was diagnosed in 110 cases, 48 per cent. In 97 additional cases it was thought likely, from the incomplete records available, that some degree of enlargement existed. An attempt to say whether or not the heart is enlarged, without complete data including the weight of the patient, the shape of the chest and a teleroentgenogram, must be, of course, only a rough estimate in many cases. It is well known, however, that cardiac enlargement is one of the most constant accompaniments of all types of chronic heart disease.

Autopsy Findings.—Unfortunately there were records of postmortem examination in only seven cases. It is notable, however, that coronary disease was found without exception in these seven instances.

Rheumatic Heart Disease.—This was conspicuous by its rarity. There were only five cases. One of these was that of a man forty-two years of age in whose case autopsy showed sclerosis of the coronary arteries.

SUMMARY OF RESULTS

Incidence.—Less than half of these patients presented themselves on account of symptoms referable to their hearts. In a considerable number of the others, however, examination and history discovered evidence of heart disease. But the total number of cases with a cardiac diagnosis (both principal and secondary) was only a little larger than the number without such a diagnosis. Only about half of the patients gave evidence of any degree of cardiac insufficiency. One factor, however, was practically constant. The incidence of these electrocardiograms was found to be confined almost exclusively to patients who had arterial disease or some other disease which brought the coronary arteries under suspicion. Investigation of their incidence, therefore, gives strong indication that coronary disease is responsible for the particular form which they assume.

RELATIONSHIP OF ETIOLOGICAL FACTORS TO THE QUESTION OF DELAYED CONDUCTION

There remains for consideration the application of the finding of coronary disease in the incidence of these records to the question of impairment of conductivity in the right limb of the A-V bundle. It

is well known, of course, that interference with the blood supply to the main stem of the A-V bundle, or to either limb, may impair conductivity in the affected part. Other lesions may produce the same result. The above findings, however, indicate that coronary disease is by far the commonest cause of such impairment in the right limb. Other considerations have an intimate bearing on the problem. The characteristic incidence of electrocardiograms showing bundle-branch block is in patients with coronary disease. It is well known that complete absence of conductivity in one branch of the bundle (bundle-branch block) occurs in the right limb with much greater frequency than in the left. Lesser defects in conductivity due to the same process would be expected to occur in somewhat the same ratio, between the right and the left limbs, as do instances of complete block. Such, indeed, appears to be the case. Investigation by one of us shows that the records in our files which might be taken to indicate impairment of conductivity in the left limb of the A-V bundle are in fact relatively quite rare among patients in the older age groups. Just how the right branch of the A-V bundle might be expected to suffer more frequently than the left branch, as a result of coronary disease, is at once apparent upon consideration of the arterial distribution to the two main limbs of the bundle. Gross[3] has shown that the right limb is invariably supplied by a branch from only one of the main coronary arteries, the left; while the septal part of the left limb of the bundle is usually (92 per cent of cases) supplied by branches from both the right and left coronaries. In only 8 per cent of cases is the septal part of the left limb supplied by a branch from only one coronary, the left. In cases of coronary disease, therefore, affecting principally the right coronary, the right limb of the A-V bundle would not suffer. Neither would the left limb suffer materially, for it always derives at least a part of its blood supply from the left coronary. In arterial disease affecting the left coronary, however, the right limb of the bundle would invariably suffer to a greater or less extent. In most such cases of left coronary disease (92 per cent) the impairment of the conducting system *would be limited to the right branch;* while in a small number of such cases (8 per cent) impairment would obtain also in the left branch of the A-V bundle. Assuming that the principal lesion of coronary disease is as likely to occur in one coronary as in the other, the ratio of incidence of conduction defects of all degrees, due to arterial disease, in the right branch of the A-V bundle to the incidence of such defects in the left branch, therefore, would be in the ratio of 92:8.

The ratio of the number of electrocardiograms indicative of right bundle-branch block to the number of records indicative of left bundle-branch block, however, is considerably higher than 92:8. This accords both with the theory of bundle-branch block as expressed by

the electrocardiogram and with the above explanation of such block. Block in one of the branches of the A-V bundle can be exhibited in the electrocardiogram only when conduction is maintained in the other branch. For if neither branch were able to transmit an impulse, the resulting electrocardiogram would exhibit, not block in one branch of the bundle, but complete A-V block. In that small group of cases (8 per cent) in which the left coronary alone supplies both the right and left branches of the bundle, instances must occur in which conduction suffers equally in the two branches. The electrocardiogram in such cases obviously will not express the defect in the left branch alone. This reduces the number of electrocardiograms which might show left bundle-branch block, and also the number which might show lesser degrees of impairment in the left branch. The result, therefore, is that the ratio of such records to those which show impairment in the right limb is lower than the arterial distribution might seem, at first thought, to indicate. In less than 8 per cent of cases of left coronary disease, then, will the electrocardiogram show defective conduction in the left bundle branch, while in more than 92 per cent of such cases will it show a conduction defect in the right branch. It follows, therefore, that not only does arterial disease offer ready explanation of impairment of conductivity, but the arterial distribution to the branches of the A-V conducting system also explains the higher incidence of this impairment in the right limb of the bundle.

Since hypertrophy (presumably of the left ventricle more than of the right) was found to be characteristic of these cases, it might be contended that these electrocardiograms express merely "left ventricular hypertrophy." We do not maintain that relative preponderance of left muscle mass is not one of the causes of left axis deviation. But it is not the only cause. And it leaves unexplained the characteristic relationship of the T-wave to the initial deflection of the ventricular complex in those instances of left axis deviation with which our paper deals. We make no attempt to offer an explanation of causes underlying the changes in electrical potential that produce the T-wave, but we emphasize the fact that in this particular type of electrocardiogram the relationship of the QRS complex to the T-wave is that of defective right bundle-branch conduction. Since this also is one of the causes of left axis deviation, and since the study of our cases indicates the occurrence of a constant factor that would be expected to impair conductivity in the right limb of the bundle, the evidence is very great that defective right bundle-branch conduction rather than some other cause of left axis deviation is responsible for the particular shape which these electrocardiograms assume.

SUMMARY AND CONCLUSIONS

The incidence of electrocardiograms showing left axis deviation and QRS of normal duration, with inverted T_1 and upright T_3, is confined almost exclusively to patients who exhibit either coronary diseases or some other disease which makes the presence of coronary involvement more or less probable.

Experimental and clinical data strongly indicate that these electrocardiograms represent impairment of conductivity in the right limb of the A-V bundle.

Consideration of the arterial distribution to the limbs of the bundle makes it appear highly probable that the conduction defect is induced by the concomitant vascular process.

Vascular lesions may be of sufficient consequence to produce such conduction defects, and electrocardiograms of this type, therefore, may be recorded before other important evidences of cardiac involvement become apparent.

The question of the influence of digitalis on the shape of these electrocardiograms, particularly so far as it concerns the inverted T-wave in Lead I, deserves comment. It is well known that digitalis produces inversion of the T-wave. It does not, however, in normal electrocardiograms, lower T_1 and, *at the same time,* elevate T_3. There is much evidence that it depresses conductivity in the bundle-branches. In cases of defective right bundle-branch conduction, therefore, such a defect might easily be increased by the drug, the characteristic electrocardiographic features being accentuated, T_1 becoming deeper and T_3 becoming higher. We have observed such results in some of our cases. Many of our patients had had digitalis at the time of their *first* electrocardiogram, many had not. Just how far digitalis may have accentuated the characteristic features in some of these records we have not attempted to determine. The importance of doing so would appear to bear only on the question of the extent of digitalis action on bundle-branch conduction, for it would appear extremely unlikely that the drug could *produce* such a defect in cases in which no impairment already existed. The defect in right bundle-branch conduction shown in our records, therefore, while accentuated by digitalis in some instances, perhaps, depends even in such cases primarily on a pathological process, and is not produced by the drug.

This conclusion is further strengthened by the following consideration: Digitalis had been administered, not only to the patients whose electrocardiograms we studied, but also to the patients whose records did not meet the criteria for selection, in (presumably) about the same proportion of cases. Yet our study shows that it was only in those patients with evidence of arterial disease that electrocardiograms were recorded which showed the exact relationship of QRS to T complexes indicative of right bundle-branch defect. Any primary effect of digitalis in producing the characteristic shape of these electrocardiograms, therefore, would appear to be very unlikely.

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THE PRE-EMPLOYMENT EXAMINATION OF THE CARDIAC WORKER*

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THE examination of the prospective employee made its appearance in industry some years ago and chiefly in those industries where there existed important hazards with reference to other persons outside of the business: such industries, for example, as railroads, street railway companies, operators of public conveyances, and other forms of service or industry where numbers of persons might be subject to the results of the acts of employees of the company rendering the service. From that point the examination of the prospective employee has gradually spread throughout the industrial world; doubtless receiving, in part, its impulse through the various forms of benefit and relief payment plans as well as from the various state compensation laws. And now we believe that the pre-employment examination has a definite place in industry, not as is often assumed for the purpose of eliminating the unfit, but for the purpose of a physical appraisal of the personnel so that the employer may know the physical "status quo" of the additions to his force.

Theoretically, the physical examination for employment should exclude only those members of society who through their physical condition constitute a hazard to themselves, to others or to property or service. The pre-employment examination should have for its purpose the recognition, the evaluation, and cataloguing of the several acceptable physical impairments of the individual and his allocation in the business according to the physical abilities to perform, as determined by the several impairments found. Under such a plan the number of rejections under ordinary conditions should be relatively few, and, furthermore, industry through its attitude toward the pre-employment group would be making a real contribution to public health in keeping with our present knowledge of social economics. There are times, however, when pre-employment rejections may become relatively numerous; such conditions as a very abundant labor market where it is easy to imagine that an industry in its physical examination plant would be obliged to pick and choose logically. Under such circumstances, it is only natural to expect that the standard of their physical requirements would be raised, and out of a large number of applicants selection made of those best suited physically for employment. This foregoing policy with reference to pre-employment examination ap-

*From the office of the Medical Director, American Telephone and Telegraph Company.
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plies with equal force when we come to consider the cardiac applicant. It is a fact that at present in many industries, the cardiac applicant, no matter what form of disease may be present, is considered "persona non grata," idealistic pre-employment examinations notwithstanding. This possibly may be due to several factors:

First, the time element. For economic reasons, the pre-employment examination must necessarily be brief. The time allotted to the average industrial plant examination is so short that a careful study of an abnormal heart cannot be made in every instance. Thus, quite general rejections where prominent impairments of any sort are found.

Second, the ability of the examiner. It is a recognized fact that the major portion of those concerned in pre-employment physical examinations are not skilled to the degree of deciding whether or not, based on their findings, they should or should not recommend the employment of a given cardiac applicant. Thus, quite often in the industrial medical department the examiner through lack of time, plus no small degree of ignorance, fails to make his contribution.

THE COMPENSATION LAWS

Industry is not altogether to be blamed for the unfortunate attitude which it has taken toward the prospective employee with a cardiac condition. It must be admitted that employers in certain states are prejudiced against the cardiac applicant no matter what the type. As the compensation commissions go more and more into the consideration of the accident problems rising out of or in the course of employment, they see many instances where, though on doubtful bases, they feel compelled to render decisions against employers, because of what they may consider as aggravated, predisposing cardiac causes to certain accidents. If, on the other hand, the industry has a definite record of the cardiac standing of a particular employee, and at the same time has a record of the type, duration, and supervision of the employment, there is then in the possession of the employer real evidence to be presented if at any time these cases as the result of accident come to the attention of the local commissions. Such evidence should be of value to commissions and assist them in arriving at decisions as to compensation.

COMPANY OR PARTICIPATING PLANS FOR SICKNESS RELIEF

In many industries of the present day where personnel problems have been thought out along sound sociological lines, there exist plans for benefits and pensions. If individuals are accepted for employment who have cardiac impairments showing signs of inevitable catastrophe within a relatively short time, it would be poor business to expend company funds in expensive training. It would likewise hardly be justifiable to place them in line to receive sickness benefit payments. Again, it is a fact of experience that persons with certain cardiac

lesions when they become the subject of acute infectious disease, have long convalescence periods and are more liable to have complicated results.

JOB PREPARATION

In some industries before a prospective employee can qualify to a normal productive capacity, there exists a rather intensive training period. This interjects ofttimes an unlooked-for feature in employment where the effort involved may be all out of proportion to that necessary after the final job assignment is made. Meanwhile, our cardiac applicant is an employee, perhaps on probation, if you please, but nevertheless he is an unusual liability in a double sense; first, that growing out of the temporary but unusual nature of the employment and, second, because of the necessarily costly nature of the instruction during the training period.

If it were possible to accept the major portion of those suffering from cardiac disease, who are in a position to go to the employment office and apply for a job, there would be an opportunity to render a service to the community, in that the industry thereby would accept its own proportion of the community's social responsibility. It would likewise be to the advantage of the acceptable cardiac worker, because such an individual immediately would have an opportunity to gain confidence in himself, which, if he has been considered a cardiac applicant for a few months and during that time has applied for employment, he has had many opportunities to have it shaken. Furthermore, in those industries maintaining medical departments, there is presented an opportunity for medical supervision to the extent of seeing that the job allotted fits into the sphere of what is acknowledged as a proper one for the given cardiac impairment. This supervision may also be exercised to the extent of insisting that the employee at proper times consult a capable family physician or resort to a well-conducted cardiac clinic.

The cardiac employee is an economic problem and if industry maintains the same attitude of stringency toward all cardiac employees, there is going to be progressive economic loss due to wastage of utilizable talent. The statement that there are two million people with heart disease in the United States is without doubt conservative. The wartime draft examinations rejected 42.3 men out of every thousand because of heart disease. Of this large number, it would be logical to say that at least 50 per cent are employable in some capacity or other.

The cardiac individual who some time in his career has the label "cardiac" tied to him is a poor advertisement for himself. He perhaps too often becomes afflicted with a certain mental twist whereby he is naturally disinclined to do those things which he either thinks or has been told will damage his already damaged heart. As a result,

there is a timidity and a tendency toward introspection and the avoidance of physical effort which ofttimes may be out of proportion to the actual cardiac state present. He then puts himself at once in a compromising position.

In fairness to industry, cardiac employees must always be considered for special or modified employment and, when considered from the standpoint of industry, they may be roughly divided into two groups:

First, those who can work without discomfort, and second, those who cannot work without discomfort.

Under this latter heading there need be no further subdivision, as industry aside from the medical standpoint cannot and should not be concerned with them.

Under the division of those who can work, we may make a number of artificial classifications:

1. Those who can work full time.

2. Those who can work on some individually determined limited time bases.

It may be possible under those classified as full time cardiac employees to subdivide still further this group under:

a. Those capable of working under conditions of ordinary limited physical or mental strain.

b. Those capable of working only under specially determined limited physical or mental strain.

In the group of individuals working under limited time, the subdivisions may be practically the same as those classified under full time cardiac employees.

In determining the acceptability of a given cardiac applicant, either on a full time or on a limited time basis, the clinical signs necessarily center about a few easily determined factors: first, the history with reference to the cause of the cardiac condition; and second, the history with reference to the result of the cardiac condition (in other words, the compensation history).

A rather brief physical survey may show both physical and auditory signs of what seems to be a present or previous decompensation catastrophe. To make this somewhat more explicit, there is not so much determinative information to be obtained through an auscultatory examination, in view of the fact that the ordinary examiner is not in a position to form an opinion with reference to employability based on the type of lesion indicated by the cardiac sounds. Of more importance are the functional phenomena, such as shortness of breath following moderate exercise, cyanosis of the lips and ears, enlargement and pulsation of superficial vessels, peripheral edema, and other signs indicating that a decompensation is well under way or may be in the process of subsidence. In determining the employment of a

given cardiac applicant, these general physical indices should be taken into account together with the character of the reestablished compensation, in order to decide, first, whether the compensation has been brought about with no functional residues, and second, if there still exists evidence in the compensation of functional residues.

How employable a prospective employee may be, as based on compensation breaks, may in a measure, rest on the number of times and the character of each pre-existing breakdown of the compensation, together with the intervening rehabilitation time.

My own impression would be that in an individual of questionable general physique who gives a history, or in whom in the course of a physical examination there exist evidences of two or more breaks, the question of employment should be deferred, perhaps to come up for reconsideration after the lapse of a reasonable period of time. Dogmatic finality should be avoided as far as possible, as these individuals need encouragement at every turn.

The cardiac applicant should also be appraised as to the amount of psychical damage that has grown out of his experience with the cardiac impairment. Many such individuals are psychoneurotic to a pronounced degree. Such cases can become a serious drain on industry through absenteeism because of occasional real and more often imaginary indisposition. Except in instances where such individuals can have more or less solitary employment, they may become real problems to their superiors, due to the effect on the morale of the rest of the group among which they may be working. It is humanly impossible over any extended period of time, in spite of real sympathy and charity in judgment, to overcome a certain element of resentment on the part of other employees who are witnesses to these necessary breakdowns in departmental routine. Furthermore, certain cardiac workers, when the victims of some acute disease process, become a further problem because of the marked extension in convalescence time.

In planning a program of pre-employment examinations, there are a number of factors to be considered, and it must be remembered that in an industry each new departure will be conducted along definite economical lines. Throughout industry in general, the funds available for the employment of physicians as examiners will not permit medical departments to hire experts in cardiac diagnosis or, indeed, little talent that could be classed as expert. Furthermore, the question of time allotment for an examination will sooner or later loom on the horizon and as medical work grows in any given industry, the various steps of the pre-employment examination and even the periodic examination will have allotted to it a time limit, not rigid of course, but indicating to the medical employee that he likewise must produce and get his product out with a certain amount of celerity. It will thus be seen that, in the course of an average pre-employment examination,

there will probably be from five to ten minutes spent on the heart examination and then only upon evidence of unusual cardiac pathology. Thus it is easy to see that the average physical appraisal of an applicant for employment who has cardiac disease must of necessity be superficial in the extreme, because of lack of special diagnostic skill, of lack of time, and of lack, if you please, of interest in the question of the pathology present (since to the average examiner such a case is not a personal patient or even an object of much concern).

The decision for or against employment must be based on a composite cardiac picture consisting of:

1. A few hard and fast rules governing the actual heart examination.
2. A brief psychical appraisal.
3. The history or evidence of present or recent decompensation.
4. The establishment of the fact that the applicant has or has not complied with clinical requirements regarding the elimination of sites of focal infection.

Once having determined that a given applicant for employment has cardiac disease, there are certain examination facts which will decide against recommendation for employment and these may be listed as follows:

1. Inspection signs of cardiac disease and accompanying decompensation or phenomena of endocrine dyscrasia.
2. Any diastolic murmur or thrill.
3. Auricular fibrillation.
4. A rate, after rest, that is persistently above 90 or below 50 or a pulsus alternans.
5. Paroxysmal tachycardia.
6. A persistent systolic blood pressure, in adults up to forty years of age, of 160 or more, or of 100 or below after complete horizontal rest for ten minutes.

An individual with cardiac disease to be employable under a special assignment schedule, as previously stated, should present no gross inspection signs of cardiac disease or decompensation following simple exercise functional tests. The cardiac murmur present should not be transmitted into the neck. Where pulse intermittency exists, it should be the result of extrasystoles and should not be accompanied by a palpable thrill or tumultuous impulse in the area of the apex beat. The rate should be within normal limits.

These few clinical data should be easily elicited by the average man doing medical department pre-employment examinations. It is felt that the exclusion of those handicapped to the extent indicated in the nonacceptable requirements would constitute a hazard in any form of employment, from the standpoint of affecting the morale of the rest of the force, their own and others health or safety, and through the limited contribution to the product or service of the particular part of the industry in which they desired to be employed.

MORTALITY AND MORBIDITY FROM HEART DISEASE UNDER INDUSTRIAL AND GROUP INSURANCE

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HEART disease and limitation of capacity for physical exertion are so closely associated, and heart disease may be so aggravated by physical exertion that it might quite naturally be assumed that the interrelations of heart disease and occupation would be reflected in high mortality rates in at least a considerable number of occupational groups. There is little evidence, however, that such excessive occupational mortality exists.

This is a matter of particular interest when it is remembered that heart disease is foremost among the causes of death. In striking contrast stand pulmonary tuberculosis, pneumonia and accidents, all of which display clearly the influence of occupation upon mortality rates.

Tuberculosis is the cause of grossly excessive mortality among such workers exposed to silicious dusts as hard rock miners, pottery workers, stone cutters and grinders and among such workers as waiters, cigar makers, laundry workers and printers (see Tables I and VI).

Pneumonia causes a still more marked excessive mortality among iron foundry workers, cordage workers, metal polishers, miners and steel workers.

Deaths from accident are more readily associated with occupation, and the very high death rates from accidental violence among electric linemen, railway workers, coal miners, structural iron workers, city firemen, roofers and others are, of course, extreme examples of the effect of occupation upon mortality.

There is undoubtedly some degree of association of social or economic status and mortality from heart disease. This is reflected in the mortality rates from this cause in the several classes of insured persons. The "ordinary" class is made up, generally speaking, of the most favored individuals; the "industrial" class is made up largely of wage earners holding small policies, and the "intermediate" class falls between.

These observations are confirmed in the last report of the Registrar General of England and Wales, 1921-1923.

It is unfortunate that the statistical data relating to deaths among those covered by group insurance and by industrial insurance are not, at present, in such form as to permit of the recognition of mortality rates by specific occupations.

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Read at the Annual Meeting of the American Heart Association, February 4, 1929.

TABLE I

OCCUPATIONS SHOWING THE HIGHEST PERCENTAGE OF DEATHS FROM SPECIFIED CAUSES OF DEATH LISTED ACCORDING TO THEIR STANDARDIZED RATIOS*

MORTALITY EXPERIENCE OF METROPOLITAN LIFE INSURANCE COMPANY ON WHITE MALE INDUSTRIAL POLICYHOLDERS 15 TO 64 YEARS. 1922-1924

TUBERCULOSIS OF THE RESPIRATORY SYSTEM		PNEUMONIA (ALL FORMS)		ACCIDENTAL OR UNDEFINED VIOLENCE	
OCCUPATION	STANDARDIZED RATIO	OCCUPATION	STANDARDIZED RATIO	OCCUPATION	STANDARDIZED RATIO
Miners (underground) excluding coal miners	182.7	Iron foundry workers	220.0	Electric linemen	280.8
Pottery workers	176.5	Cordage and hemp mill workers	185.0	Railway enginemen and trainmen	240.0
Stone cutters	144.4	Polishers (iron and steel products)	183.8	Coal miners (underground)	227.5
Waiters and hotel servants	140.7	Coal miners (underground)	150.0	Structural iron workers	218.3
Cutlers and grinders	135.8	Iron and steel mill workers	142.5	Firemen (city department)	196.7
Cigar makers and tobacco workers	135.2	Rubber factory workers	135.0	Roofers	188.3
Laundry workers	134.6	Hucksters and peddlers	132.5	Fishermen, oystermen, sailors and marine workers	185.0
Compositors, printers and pressmen	130.9	Roofers	131.3	Miners (underground) excluding coal miners	184.2
Brass foundry workers	126.5	Longshoremen and stevedores	130.0	Railway track and yard workers	176.7
Barbers and hairdressers	125.9	Brick, tile and terra cotta workers	127.5	Chemical and explosives factory workers	173.3
Glass workers	123.5	Boiler makers	123.8	Cement and lime workers	170.0
Clerks, bookkeepers and office assistants	122.8	Glass workers	120.0	Oil refinery workers	160.8
Polishers (iron and steel products)	122.2	Laborers	120.0	Brick, tile and terra cotta workers	160.0
Shoe factory workers	118.5	Blacksmiths	120.0	Chauffeurs	145.8
Tailors and other clothing workers	118.5	Miners (underground) excluding coal miners	117.5	Watchmen and guards	145.0
Furniture and other woodworkers	118.5	Stone cutters	117.5	Saw and planing mill workers	143.3
Cordage and hemp mill workers	117.9	Street and sewer cleaners	115.0	Electricians	143.3
Slaughter and packing house workers	117.9	Masons and bricklayers	113.8	Paper and pulp mill workers	140.8
Shoemakers (cobblers)	116.7	Cement and lime workers	111.3	Longshoremen and stevedores	137.5
Bakers	116.0	Oil refinery workers	110.0	Carpenters	128.3
All occupations (excluding retired)	100.0	All occupations (excluding retired)	100.0	All occupations (excluding retired)	100.0

*The percentage of deaths from each specified cause of death in the the age period 15 to 64 years among all occupations combined was taken as 100. The standardized percentage for each cause in each occupation divided by the corresponding percentage for all occupations combined gives the standardized ratio.

Group insurance is of relatively recent development. It is written at extraordinarily low rates because there are eliminated from the transactions all possible administrative and selective procedures. Precise statements concerning the occupations of those insured are not required. In consequence the mortality which is experienced relates to industries and not to occupations. Physical examinations are not required so there is no physical selection of lives. Among those exposed to risk are individuals of varying ages, of either or both sexes, and to some extent, white or colored. It is evident that as group insurance covers employees upon the payrolls of the respective insured

TABLE II

DEATH RATES FROM OTHER DISEASES OF THE HEART
METROPOLITAN LIFE INSURANCE COMPANY, 1927
DEATHS PER 100,000 LIVES EXPOSED AT SPECIFIED AGES

AGE PERIOD	ORDINARY CLASS (MALES)	INTERMEDIATE CLASS (MALES)	INDUSTRIAL CLASS (WHITE MALES)
20 to 24 years	11.2	12.6	20.5
25 to 34 years	10.9	18.3	38.3
35 to 44 years	27.9	52.1	90.0
45 to 54 years	118.6	195.8	284.0
55 to 64 years	343.9	427.8	738.4
65 to 74 years	1013.9	1171.3	1785.8
75 years and over	3168.6	4166.7	4295.2

TABLE III

STANDARDIZED MORTALITY OF THE FIVE SOCIAL CLASSES AND OF ALL MALES. AGES 20 TO 65 YEARS
"VALVULAR DISEASE" OF THE HEART AND "OTHER HEART DISEASE"
REPORT OF THE REGISTRAR GENERAL FOR ENGLAND AND WALES, 1921-1923

	SOCIAL CLASS*					ALL MALES
	I	II	III	IV	V	
Valvular disease of heart	36.1	57.2	61.1	67.3	80.9	63.9
Other heart disease	69.7	71.6	59.0	60.4	75.6	64.9

*Social Class I—Upper and Middle.
Social Class II—Intermediate.
Social Class III—Skilled Workers.
Social Class IV—Intermediate.
Social Class V—Unskilled Workers.

groups, there is a tendency to eliminate from the exposure those individuals whose incapacity because of heart disease is such as to prevent them from engaging in active work. A portion of those incapacitated because of heart disease may, under group insurance, become eligible for total and permanent disability benefits. Such cases are charged as claim losses as of the dates of acceptance of the claims. Unfortunately, published statements of group claim experience do not offer a classification of such permanent and total disability claims, by cause. About 15 per cent are due to heart disease.

Accepting such data as are available in connection with the mortality from heart disease among the several million workers covered under group insurance, it is apparent that there exist relatively unim-

portant differences between the major classifications, such as "mining," "iron, steel and other metals," "transportation," "clerical," and "all others." Such differences as are observable in the several rates for each age are for the greater part to be explained by elements of selection incident to the demands of the respective industrial classifications. The cardiac cripple will, for example, be almost automatically excluded from a heavy occupation. The operation of such tendencies has evidently been responsible for the levelling of cardiac mortality rates among the various occupational classes.

TABLE IV

DISEASES OF HEART AND CIRCULATORY SYSTEM
DEATHS PER 100,000 LIFE YEARS

CENTRAL AGE	MINING	IRON, STEEL OTHER METALS	TRANSPORTATION	CLERICAL	ALL OTHERS
	Class I	Class II	Class III	Class IV	Class V
18	14.0	6.2	16.6	19.8	21.3
23	23.8	26.8	23.8	13.8	21.5
28	34.6	31.6	29.7	28.4	25.6
33	46.8	45.9	39.7	32.8	38.5
38	45.2	73.9	76.6	53.2	65.5
43	112.9	122.8	133.2	95.9	111.5
48	188.3	177.1	229.1	184.7	185.1
53	316.5	344.9	361.3	356.2	296.8
58	505.7	529.6	594.2	546.6	515.7
63	765.6	816.6	1020.2	1000.0	872.9
68	1325.3	1600.0	1774.3	1551.1	1386.2
73	1293.1	2552.6	2556.6	2394.7	1956.6
78	2991.4	4354.8	4655.1	4114.3	3273.7
83	3333.3	6611.5	6666.6	5431.3	6257.2
88	5263.1	10000.0	9230.7	3571.4	7260.6

At the present time group insurance data concerning morbidity from heart disease in relation to occupation are not to be had. It is possible, however, to present some general figures indicating the relative importance of diseases of the circulatory system among the many causes of illness for which benefits are payable in time of sickness.

In a study of 6671 claims incurred under policies paying benefits for approximately twenty-six weeks beginning on the eighth day of illness among white males, a life year exposure of 173,000 years, there were 323 or 4.8 per cent of the total number paid for losses due to various types of circulatory diseases, about 2 per 1,000. These claims involved the payment of 9 per cent of the total benefits paid for all causes and were of an average duration of 75.7 days which may be compared with an average duration of benefit of 41 days, and which is a greater duration than that associated with any other group of disabilities.

Among white females under similar policy provisions, 34,000 life years, the diseases of the circulatory system accounted for 32 claims out of 1154 or 2.8 per cent of the total, about 1 per 1,000; on these claims were paid 5.9 per cent of all benefits paid; and the average duration of benefit was 80.8 days which may be compared with an

average duration of benefit of 44 days. The average duration of disability due to circulatory diseases in this instance also was greater than that due to any other cause.

In view of the many circumstances which would incline the vital statistician to view group insurance mortality data as treacherous and untrustworthy, it is of interest that an extensive mortality experience among men covered by that form of insurance known as industrial insurance shows an almost identical picture.

These data relate to deaths among individual policyholders whose occupations at death are recorded. Unfortunately, the number of lives at risk in each occupational classification cannot be obtained, so true death rates are not available. In consequence it is necessary to resort to the use of a form of statement of mortality, which, while useful and truly informative, leaves much to be desired. The proportion of deaths from any cause, such as heart disease, in an occupational group is corrected for age and expressed in ratio to the proportion of deaths from that cause among all occupied males. This figure is known as the "standardized ratio."

In a study recently undertaken by the Statistical Bureau of the Metropolitan Life Insurance Company, under the direction of Dr. Louis I. Dublin, there was determined the relation of occupation to 105,467 deaths which occurred during the three years, 1922 to 1924, among three and one quarter million male white industrial policyholders.

The great majority, 90 per cent, of cardiac deaths were due to the cause of the international classification known as "Other Diseases of the Heart," heart disease excluding pericarditis, acute endocarditis, acute myocarditis, and angina pectoris.

TABLE V

NUMBER OF DEATHS IN SPECIFIED AGE PERIODS FROM ALL CAUSES AND FROM "OTHER DISEASES OF THE HEART." MORTALITY EXPERIENCE OF METROPOLITAN LIFE INSURANCE COMPANY ON WHITE MALE INDUSTRIAL POLICYHOLDERS (EXCLUDING RETIRED) 15 YEARS AND OLDER, 1922 TO 1924

CAUSES OF DEATH	NUMBER OF DEATHS						
	AGES 15 YEARS AND OVER	15 TO 24 YEARS	25 TO 34 YEARS	35 TO 44 YEARS	45 TO 54 YEARS	55 TO 64 YEARS	65 YEARS AND OVER
All causes	105,467	11,927	12,153	15,041	19,656	25,054	21,636
Other diseases of the heart	16,217	903	854	1,386	2,982	4,941	5,151

To this cause, "Other Diseases of the Heart," were assigned 16,217 deaths of individuals fifteen years or over, and it is to this class that the following data relate. The standardized ratios were computed for those deaths between the ages of fifteen and sixty-four years.

With the "ratio" of 100 for all occupied males, those for specific occupations ranged, strangely enough, from 180 among sailors of the navy to 37 among soldiers. These ratios may be ignored, however, as they

TABLE VI

PERCENTAGE OF DEATHS DUE TO "OTHER DISEASES OF THE HEART" OF DEATHS FROM ALL CAUSES IN SPECIFIED OCCUPATIONS
MORTALITY EXPERIENCE OF METROPOLITAN LIFE INSURANCE COMPANY ON WHITE MALE INDUSTRIAL POLICYHOLDERS 15 YEARS AND OLDER.
1922 TO 1924.

OCCUPATION OR INDUSTRY	DEATHS (15 YEARS AND OLDER)		PERCENTAGE OF DEATHS FROM OTHER DISEASES OF THE HEART		STANDARDIZED RATIO*
	ALL CAUSES	OTHER DISEASES OF THE HEART	CRUDE FOR AGES 15 YEARS AND OLDER	STANDARDIZED FOR AGES 15 TO 64 YEARS	AGES 15 TO 64 YEARS
All occupations combined (excluding retired)	105,467	16,217	15.4	13.2	100.0
Sailors (navy)	218	10	4.6	23.8	180.3
Boiler makers	367	64	17.4	17.0	128.8
Merchants and storekeepers	3,133	578	18.4	16.9	128.0
Roofers	179	26	14.5	16.3	123.5
Cooks (hotel and restaurant)	324	59	18.2	16.3	123.5
Tailors and other clothing workers	1,175	232	19.7	16.2	122.7
Textile dyeing, bleaching, and finishing mill workers	391	81	20.7	15.5	117.4
Waiters and hotel servants	789	127	16.1	15.4	116.7
Clerks, bookkeepers and office assistants	5,140	749	14.6	15.2	115.2
Barbers and hairdressers	768	132	17.2	14.8	112.1
Shoemakers (cobblers)	666	145	21.8	14.7	111.4
Hostlers and stablemen	363	77	21.2	14.7	111.4
Brick, tile and terra cotta workers	199	36	18.1	14.6	110.6
Hucksters and peddlers	932	171	18.3	14.6	110.6
Plasterers	354	62	17.5	14.5	109.8
Janitors and building employees	2.243	446	19.9	14.5	109.8
Store clerks and salesmen	3,302	490	14.8	14.4	109.1
Agents, canvassers and salesmen	1,296	212	16.4	14.1	106.8
Tinners (shop) and tinware workers	467	84	18.0	14.1	106.8
Longshoremen and stevedores	594	96	16.2	14.0	106.1

*The percentage of deaths (13.2) shown in column 4 for all occupations combined was taken as 100. The standardized percentage for each occupation divided by 13.2 gives the *Standardized Ratio.*

are based upon small numbers of deaths and being corrected for age do not accurately reflect the actual incidence of cardiac deaths in these two highly selected occupational groups.

These ratios, it must be clearly understood, are not death rates. They reflect only the importance of cardiac mortality in relation to other causes. Such indices, however, are of value in disclosing any tendency of occupation to induce an excessive mortality from any cause or causes.

The best extensive occupational mortality data of recent date now available are to be found in the report of the Registrar General of England and Wales for the period 1921-1923.

Among 164 occupational classes of those males dying between the ages twenty and sixty-five years but 16 classes showed significant standardized mortality rates from valvular diseases of the heart in excess of that for all occupied and retired males, and 21 classes, an excessive mortality from "Other Diseases of the Heart."

In only a few classes was the excess mortality at all marked. It was for other diseases of the heart particularly notable in those classes exposed to a silica hazard and with bartenders. The association of heart disease and a silica hazard was not evident in the American data.

It is possible, even probable, that there is in this country a higher degree of mobility of labor than in Great Britain, a greater tendency of workers to shift from one form of employment to another more congenial or better suited to physical capacity.

It may thus be seen that whatever may be the importance of the part played by occupation in the development or aggravation of cardiac incapacity in particular, individual cases, there is no considerable evidence that certain occupations are conducive to high death rates in the battle with the new captain of the men of death.

STATISTICAL STUDIES BEARING ON PROBLEMS IN THE CLASSIFICATION OF HEART DISEASES

V. Heart Disease Among Ex-Service Men*†

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(Continued from page 313, February issue)

DEATHS FROM CARDIOVASCULAR DISEASE

The data received from the hospitals indicated that 60 beneficiaries died from cardiovascular disease. It was thought that it might prove of value to analyze these deaths for the purpose of ascertaining the etiological factor of the heart disease, the age of the patient at death, and the specific lesion or lesions causing death. These facts are brought out in Tables XIV, XV, and XVI, which follow:

Table XIV lists a series of 60 patients who had been under treatment for various cardiovascular diseases and who died. The cardiovascular lesions are arranged according to etiology as well as to specific diagnosis. These 60 patients gave a history of having had 100 cardiovascular lesions, the latter being due to 116 factors. It is thus seen that the average number of lesions per patient was 1.6 and the average number of factors per patient was 1.9.

Thirty-four, or 29.31 per cent, of the lesions were of rheumatic origin; 21, or 18.10 per cent, were sequelae of infectious diseases; 14, or 12.07 per cent, were syphilitic; and in 37, or 31.90 per cent, of the lesions, the etiological factor was unknown.

Of the total number of lesions, namely 100, the most frequent were: chronic myocarditis, enlargement of the heart, aortic insufficiency, mitral insufficiency, and mitral stenosis, in the order named.

The 60 patients referred to in Table XIV are again listed in Table XV so as to indicate the direct cause of death as well as the age at death. It is noted that 32, or 53 per cent, of the patients died from organic disease of the heart; 13 from pulmonary tuberculosis; and 4 from acute endocarditis.

While, in a number of cases, the cardiovascular disease was not the direct cause of death, in 32, or 53 per cent, of the group the disease of the heart was the primary cause of death. It is probable that in those

*From the Research Subdivision Medical Service, U. S. Veterans Bureau, and from the Research Committee of the Heart Committee of the New York Tuberculosis and Health Association.

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TABLE XIV

DEATHS OF 60 CARDIAC PATIENTS, BY SPECIFIC DISEASE, AND BY ETIOLOGICAL TYPE OF HEART DISEASE

SPECIFIC DISEASE	RHEUMATIC	SEQUELAE OF INFECTIOUS DISEASES	SYPHILITIC	TOXIC	GENERAL SYSTEMIC DISEASE	THYROID	OTHERS	UNKNOWN	TOTAL ETIOLOGICAL FACTORS	TOTAL HEART LESIONS
Myocarditis, chronic	6	3	1	3	1			4	18	14
Enlargement of heart	3	4						8	15	14
Cardiac valvular disease, aortic insufficiency	6	2	3					3	14	13
Cardiac valvular disease, mitral insufficiency	1	2	2					7	12	12
Cardiac valvular disease, mitral stenosis	6	2				1		2	11	10
Hypertrophy of heart	1	2			1			4	8	7
Aortitis, without dilatation	1		4						5	5
Endocarditis, acute	2						1	1	4	4
Thrombosis of femoral, saphenous and popliteal veins		2					1		3	1
Auricular fibrillation		2						1	3	3
Heart-block	2	1							3	1
Arrhythmia	2	1							3	1
Myocarditis, acute	1			1					2	1
Fatty degeneration of heart								2	2	2
Arteriosclerosis, general			1					1	2	2
Cardiac valvular disease, aortic stenosis	1		1						2	2
Hypertension	1				1				2	1
Fatty infiltration of heart								1	1	1
Tumor of pericardium			1						1	1
Aneurysm of aorta			1						1	1
Aneurysm of pulmonary artery								1	1	1
Aneurysm of ulnar artery	1								1	1
Thrombosis of veins of pelvis and legs								1	1	1
Endocarditis, chronic								1	1	1
Total	34	21	14	4	3	1	2	37	116	100
Per cent	29.31	18.10	12.07	3.45	2.59	0.86	1.72	31.90	100.00	

TABLE XV

DEATHS OF 60 CARDIAC PATIENTS BY DIRECT CAUSE AND AGE AT DEATH

DIRECT CAUSE OF DEATH	22-23	24-25	26-27	28-29	30-31	32-33	34-35	44-45	46-47	50-	AGE NOT STATED	TOTAL
Organic diseases of the heart		2	2	1	4	1		1	2	2	17	32
Tuberculosis of the lungs	1	1	1	1	3	1	3				2	13
Endocarditis, acute		2									2	4
Hemorrhage; other diseases of the circulatory system							1			1	1	3
Diseases of the arteries, atheroma, aneurysm, etc.											2	2
Bright's disease											2	2
Pott's disease				1								1
Cancer and other malignant tumors of other organs or of organs *not specified*						1						1
Pulmonary congestion, *pulmonary apoplexy*											1	1
Diseases of the stomach (cancer excepted)											1	1
Total	1	5	3	3	7	3	4	1	2	3	28	60

TABLE XVI

SHOWING THE PRIMARY CARDIOVASCULAR DISEASE FOR WHICH 60 EX-SERVICE PATIENTS WERE HOSPITALIZED AND WHO DIED DURING HOSPITAL STAY

CARDIOVASCULAR DISEASES	AGE OF DEATH										
	22-23	24-25	26-27	28-29	30-31	32-33	34-35	44-45	46-47	50-	NOT STATED	TOTAL
Myocarditis, chronic, fibrous					2			1	1	1	1	6
Enlargement of heart			1		1	1	1					4
Endocarditis, acute		1					1				2	4
Mitral stenosis					1					1	2	4
Aortic insufficiency						1					2	3
Mitral insufficiency and mitral stenosis									1		2	3
Enlargement of heart and hypertrophy of heart					1		1					2
Enlargement of heart and myocarditis, chronic, fibrous				1							1	2
Enlargement of heart and fatty degeneration	1					1						2
Myocarditis, chronic, fibrous and auricular fibrillation			1				1					2
Aortic insufficiency and aortic stenosis				1							1	2
Mitral insufficiency											2	2
Enlargement of heart, hypertrophy of heart, and myocarditis, chronic, fibrous											1	1
Enlargement of heart and chronic endocarditis											1	1
Enlargement of heart and aortic and mitral insufficiency			1									1
Enlargement of heart and mitral insufficiency					1							1
Hypertrophy of heart, myocarditis, chronic, fibrous, and fatty infiltration											1	1

TABLE XVI—CONT'D

CARDIOVASCULAR DISEASES	AGE OF DEATH											
	22-23	24-25	26-27	28-29	30-31	32-33	34-35	44-45	46-47	50-	NOT STATED	TOTAL
Hypertrophy of heart, myocarditis, chronic, fibrous, and hypertension											1	1
Hypertrophy of heart and aortic insufficiency.											1	1
Hypertrophy of heart and mitral insufficiency		1										1
Myocarditis, acute											1	1
Myocarditis, chronic, fibrous, heart-block and arrhythmia										1		1
Tumor of pericardium and aortitis without dilatation											1	1
Aortitis and aneurysm of aorta											1	1
Aortitis and arteriosclerosis, general											1	1
Aortitis and aortic insufficiency		1										1
Aortitis and aortic and mitral insufficiency											1	1
Aneurysm of pulmonary artery		1										1
Aneurysm of ulnar artery, aortic insufficiency, and mitral stenosis		1										1
Thrombosis of femoral, saphenous, and popliteal veins											1	1
Thrombosis of veins of pelvis and legs				1								1
Arteriosclerosis, general											1	1
Aortic and mitral insufficiency											1	1
Aortic insufficiency and mitral stenosis											1	1
Mitral insufficiency, heart-block and arrhythmia					1							1
Mitral stenosis and auricular fibrillation											1	1
Total	1	5	3	3	7	3	4	1	2	3	28	60

cases where death was not directly due to cardiovascular disease, the latter might have been a contributing factor.

Table XVI is a compilation of the 60 cases referred to in Tables XIV and XV arranged according to the specific cardiovascular disease for which they were hospitalized and according to the age at death. Attention is again invited to the fact that even though cardiovascular disease existed at the time, it was not necessarily a primary cause of death, but may have been a contributory factor.

It has been pointed out by Dublin, and also by Cohn, that five-sixths of the deaths from heart disease take place after the age of forty, while only one-sixth of the deaths occur prior to that age.

The data in Table XVI indicate that of the total of 60 cases the age at death of 28 is not stated. In the series of 32 cases, in which the age at death was recorded, it is noted that 6 were between forty-four and fifty years of age; 26 between the ages of twenty-two and thirty-five; 7 died at the age of thirty or thirty-one; 4 died at the age of thirty-four or thirty-five; and 5 died at the age of twenty-four or twenty-five. These figures are not of particular significance in view of the fact that the group as a whole is a select one and the average age of these patients is approximately thirty-six years.

A study of the specific heart lesions for which these patients were hospitalized indicates that 25, or 41.67 per cent, of the patients had some chronic valvular disease of the heart.

Mortality Rate From Cardiovascular Disease in the U. S. Veterans Bureau, Fiscal Years 1922-1926, Inclusive.—An attempt was made to analyze the deaths in the Veterans Bureau from cardiovascular disease during the period, 1922 to 1926. Reference to Table XVII shows that the number has increased from year to year with the exception of 1924, in which year there was a material decrease in deaths due to this cause. There were 98 deaths in 1922, 192 in 1923, 147 in 1924, 206 in 1925, and 296 in 1926. The total deaths in Bureau and other hospitals from cardiovascular disease for these years was 939. The total deaths from all causes for the same period was 12,718, making the percentage of deaths due to cardiovascular disease for this period 7.38.

These figures may be compared with the observations of J. S. Whitney[10] who found that the mortality from heart disease in the civil population was 15 per cent of all deaths every year.

An attempt was made to ascertain the primary cause of death among the 939 patients dying from cardiovascular disease during 1922-1926, inclusive. Reference to Table XVIII indicates that in 661, or 70.4 per cent, of the cases the primary cause of death was organic disease of the heart.

Age at Death.—J. S. Whitney[10] found that the mortality rate of cardiac patients of the civil population is least at the ages from twenty to twenty-four years, and highest at the ages from seventy-five to seventy-nine. Dublin[2] states that heart disease is preëminently a condition of the older ages of life; but it is by no means to be neglected as a cause of death in the early years. In 1924 the Metropolitan Life Insurance Company recorded close to 20,000 deaths from heart disease among its policy holders. Of this number, 1600, or 8 per cent, were persons under the age of twenty-five years, and 3400, or 17 per cent, were under the age of forty.

TABLE XVII

YEAR	TOTAL DEATHS	DEATHS FROM CARDIO-VASCULAR DISEASE	PER CENT
1922	1299	98	7.54
1923	2639	192	7.28
1924	2502	147	5.88
1925	2866	206	7.19
1926	3412	296	8.68
Total	12718	939	7.38

TABLE XVIII

DEATHS FROM CARDIOVASCULAR DISEASES, 1922-1926, INCLUSIVE

DISEASE	1922	1923	1924	1925	1926	TOTAL
Organic disease of the heart	60	135	98	158	210	661
Acute endocarditis	7	18	6	14	19	64
Embolism and thrombosis	7	16	16	7	18	64
Hemorrhage and other diseases of the circulatory system	21	13	11	6	10	61
Diseases of the arteries, atheroma, aneurysm, etc.	1	2	6	16	26	51
Pericarditis	2	4	6	2	10	24
Angina pectoris		4	1	1	1	7
Diseases of the lymphatic system (lymphangitis, etc.)			2	2	1	5
Diseases of the veins (varices, hemorrhoids, phlebitis, etc.)			1		1	2
Total	98	192	147	206	296	939

Cohn[1] refers to a group of 954 deaths due to heart disease of which number 93.2 per cent were forty years old and over. This observer maintains that the increased rate of death from heart disease involves persons over the age of forty. Under this age the mortality rate has fallen. Cohn avers that the increased death rate from cardiovascular disease in persons over forty is predominantly due to senescent changes.

A study of Table XIX reveals the fact that of the total of 939 deaths due to cardiovascular disease, occurring during 1922-1926 among U. S. Veterans Bureau beneficiaries hospitalized in government and civil hospitals, 313 took place before the age of thirty; 438 oc-

curred within the age group from thirty to thirty-nine; 99 deaths occurred within the age group from forty to forty-nine; 43 deaths occurred within the age group from fifty to fifty-nine; and 46 deaths occurred after the age of sixty. It is thus seen that 46.6 per cent of the total number of deaths occurred within the age group from thirty to thirty-nine. The percentage of deaths from then on became less in the various succeeding age groups. Further study of the statistics in Table XIX reveals the fact that 751 of the total number of 939 patients died before the age of forty, while 188 died after that age.

This is not in accordance with the customary experience in civil life where the death rate from heart disease increases with age, but is to be expected in view of the fact that the average age of the ex-service man is thirty-six, and the age at death of most of these men falls within the various age groups twenty to thirty-nine.

TABLE XIX

DEATHS OF U. S. VETERANS BUREAU PATIENTS IN HOSPITALS FROM CARDIOVASCULAR DISEASE BY AGE AND PRIMARY CAUSE OF DEATH, FISCAL YEARS 1922-1926 INCLUSIVE

AGE AT DEATH	CARDIOVASCULAR DISEASE AS A PRIMARY CAUSE OF DEATH									
	ORGANIC DISEASES OF THE HEART	ACUTE ENDOCARDITIS	EMBOLISM AND THROMBOSIS	HEMORRHAGE, OTHER DISEASES OF THE CIRCULATORY SYSTEM	DISEASES OF THE ARTERIES, ATHEROMA, ANEURYSM, ETC.	PERICARDITIS	ANGINA PECTORIS	DISEASES OF THE LYMPHATIC SYSTEM (LYMPHANGITIS, ETC.)	DISEASES OF THE VEINS (VARICES, HEMORRHOIDS, PHLEBITIS)	TOTAL
Under 20	1			1						2
20-21	7	1	2							10
22-23	13	4		4		2				23
24-25	32	10	2	5	2	2	1			54
26-27	62	5	8	10	1	3				89
28-29	100	10	8	10	3	2	1	1		135
30-31	78	10	12	5	7	3	1			116
32-33	80	6	6	8	4	2		2	2	110
34-35	67	6	9	4	1	2	1	1		91
36-37	49	5	9	3	2	1				69
38-39	36	2	3	2	6	3				52
40-41	14	1		1	1	1	1	1		20
42-43	8		1	2		1				12
44-45	12	1	1		2	1	2			19
46-47	22			1	1					24
48-49	17		2	1	3	1				24
50-51	8				1					9
52-53	10			1	1					12
54-55	2	1		1	3					7
56-57	6		1		1					8
58-59	5	1			1					7
60-61	9			2	1					12
62-63	3				2					5
64-65	1				2					3
Over 65	19	1			6					26
Total	661	64	64	61	51	24	7	5	2	939

Deaths From Organic Disease of the Heart.—In view of the fact that 661 of the 939 deaths were due to organic heart disease it was felt that an analysis should be made of these deaths, classifying them according to the specific diagnosis and according to the age at death.

It is found that of the 661 cases the cause of death in 128 was chronic myocarditis; in 120, mitral insufficiency; in 99, combined aortic and mitral lesions; and in 82, acute cardiac dilatation.

Further study of Table XX indicates that 524, or 79.2 per cent, of the 661 deaths occurred before the age of forty, and 137, or 20.8 per cent, occurred after that age. The explanation for this has already been given in the discussion of Table XIX.

In reviewing the data compiled in Table XX it is noted that chronic myocarditis constitutes the principal cause of death from organic disease of the heart, followed by mitral insufficiency, combined aortic and mitral disease, acute cardiac dilatation, valvular heart disease, unclassified, aortic insufficiency, and mitral stenosis, in the order named.

Deaths From Cardiovascular Disease of Insured U. S. Veterans Bureau Beneficiaries.—A study was made of the mortality statistics of insured U. S. Veterans Bureau beneficiaries for the purpose of ascertaining the cause of death and the average age at death of ex-service men who had had cardiovascular disease. It was found that of 1845 deaths due to cardiovascular disease, mitral insufficiency was the cause 498 times; acute cardiac dilatation, 324 times; cerebral hemorrhage, 302 times; chronic myocarditis, 216 times; acute endocarditis, 179 times; combined aortic and mitral disease, 122 times; acute myocarditis, 104 times, and chronic endocarditis, 100 times.

Two hundred and fifty-two of the total number of 1845 insured beneficiaries were studied for the purpose of ascertaining the average age at death. It was found that the average age at death of those with acute cardiac dilatation was thirty-four years; acute endocarditis, thirty-two years; chronic endocarditis, thirty years; cerebral hemorrhage, thirty-seven years; acute myocarditis, thirty-two years; chronic myocarditis, thirty-three years; combined aortic and mitral disease, thirty-four years, and mitral insufficiency, thirty-five years.

ECONOMIC ASPECT OF HEART DISEASE

Awards for compensation are based upon the percentage evaluation of the average impairments of earning capacity resulting from the disability "in civil occupations similar to the occupation of the injured man at the time of enlistment." Impairment in ability to secure employment is also considered.

TABLE XX

CLASSIFICATION OF DEATHS FROM HEART DISEASE BY SPECIFIC DIAGNOSIS AND AGE

AGE AT DEATH	ORGANIC DISEASE OF THE HEART														
	MYOCARDITIS, CHRONIC	VALVULAR HEART DISEASE, MITRAL INSUFFICIENCY	VALVULAR HEART DISEASE, COMBINED LESIONS, AORTIC AND MITRAL	DILATATION, CARDIAC, ACUTE	VALVULAR HEART DISEASE, OTHERWISE UNCLASSIFIED	VALVULAR HEART DISEASE, AORTIC INSUFFICIENCY	VALVULAR HEART DISEASE, MITRAL STENOSIS	ENDOCARDITIS, CHRONIC	VALVULAR HEART DISEASE, AORTIC STENOSIS	DILATATION, CARDIAC, CHRONIC	CARDIAC HYPERTROPHY AND DILATATION	ANEURYSM, AORTIC	CARDIAC HYPERTROPHY	VALVULAR HEART DISEASE, TRICUSPID LESIONS	TOTAL
Under 20						1									1
20-21	1	1		1	3			1							7
22-23	1	2		2	2	3	1	1		1					13
24-25	2	7	5	3	5	3	1	4	1		1				32
26-27	5	9	14	13	12	5	2	1	1						62
28-29	9	21	12	17	12	8	12	7			2				100
30-31	16	24	9	4	9	7	5		1	2		1			78
32-33	13	11	13	10	10	7	5	8	1	1			1		80
34-35	15	10	12	11	7	6		3	2		1				67
36-37	9	6	9	7	5	6	1	2	1			2		1	49
38-39	11	8	6	4	4	1	2								36
40-41	4	3	2	1	1	2	1								14
42-43	1	1	1	1	2	1		1							8
44-45	2	3	4			2			1						12
46-47	8	3	4		2	3			1		1				22
48-49	5	1	2	1	2	1	2	1		1		1			17
50-51	3	1		1	1	1	1								8
52-53	4		1	1		2		1		1					10
54-55		1		1											2
56-57	4			1		1									6
58-59	3			2											5
60-61	4	1	1			2			1						9
62-63	1	2													3
64-65		1													1
Over 65	7	4	4	1	1	1		1							19
Total	128	120	99	82	78	63	33	31	10	6	5	4	1	1	661

Most diagnoses of heart disease were made by designated examiners employed by the Bureau, though a considerable number of such diagnoses were made by heart specialists on duty in the regional office dispensaries of the Bureau.

Observation of the types of heart examinations made by designated examiners in the field indicated such diversity of methods, particularly in exercise tests, that the Bureau prescribed a standardized heart examination for uniform employment by field examiners.[11]

The Rating of Disabilities From Diseases and Injuries.—In accordance with the provisions of Section 202, Subsection 4, World War Veterans Act, approved June 7, 1924, a schedule, taking cognizance of the occupation of the injured veteran at the time of enlistment, was prepared by the United States Veterans Bureau.

Prior to the said provision of law, the Schedule of Disability Ratings of the United States Veterans Bureau was based solely upon averages, with no recognition of occupation of the individual claimant. The preparations of the Schedule of Disability Ratings, under the terms of the Act of June 7, 1924, required pioneering effort on the part of the United States Veterans Bureau. There were few, if any, precedents available upon which to base the necessarily highly complicated and technical evaluations of disabilities as influenced by the extraordinarily large number of occupations in the United States.

The Schedule of Disability Ratings now in use by the United States Veterans Bureau and put into effect January 1, 1926, consists of two tables, which are independent and interdependent: Table I, a list of Occupational Ratings, and Table II, of Disability Ratings.

Table I is an alphabetically arranged list of occupations, a representative cross-section of the various activities in agriculture, mining, commerce, professions, etc., of American life. There are one thousand of these selected occupations. Opposite each occupation appear seventeen variants, representing various body parts, indicating estimates of the relative functional importance of the body part concerned, with respect to the occupation in question.

The diseases of the heart and pericardium are included under the caption "Chest," general arteriosclerosis comes under the caption "Systemic"; while localized arteriosclerosis would fall under the part of the body affected, as for instance chest, leg, arm, etc.

If the established occupation of the claimant at the time of enlistment does not appear in the list, an inquiry is made of the claimant regarding the type and functional requirements of his occupation, and the examiner selects a similar occupation from the list.

Table II consists of a list of injuries and diseases arranged, to facilitate reference, into separate tables, as follows:

1. Amputations, fractures, deformities, and their sequelae
2. Dental and oral
3. Eye, ear, nose, and throat
4. General medicine
5. Neuropsychiatric
6. Respiratory system and tuberculosis, pulmonary and other forms
7. Surgical
8. Combined table

Opposite the list of diseases and injuries there appear a series of nine occupational variants which are determined by and are carried over from the ratings in Table I.

Use of the Tables.—Since the introduction of this Schedule of Ratings in 1926, it has worked satisfactorily in the adjudication of compensation claims of disabled ex-service men.

The regular members of the Regional Rating Board, in cooperation with the Adjudication Division of the regional office, determine the occupation of the claimant at the time of enlistment, before the medical rating is assigned. The occupation given in the record of the Adjutant General's Office or the Bureau of Medicine and Surgery of the United States Navy is accepted.

The occupation at the time of enlistment having been satisfactorily determined, the disease or injury is next ascertained. Thereupon the medical examiner first refers to Table I, locating the appropriate occupation. The disease or injury in the case is then considered with regard to the injury variants. The figures occurring at the reading junction of the occupations with the applicable injury variants are references to the occupational variants (1-9) in Table II. Turning to Table II, the medical examiner reads and assigns the percentage of disability occurring at the reading junction of the injury list and the column reference (from 1-9) given in Table II.

Multiple disabilities are combined in accordance with the instructions in the Combined Rating Table of the Schedule.

In the adjudication of the claims for compensation the following terms are used to signify the extent of disability as well as the degree of impairment:

1. Temporary Partial (T. P.)—a disability of a temporary nature in which the degree of impairment of earning capacity may be from 10 per cent up to and inclusive of 99 per cent.

2. Permanent Partial (P. P.)—a disability of a permanent nature in which the degree of impairment of earning capacity may be from 10 per cent up to and inclusive of 99 per cent.

3. Temporary Total (T. T.)—a disability of a temporary nature in which condition there is 100 per cent of disablement.

4. Permanent Total (P. T.)—a disability of a permanent nature in which the disablement is equivalent to 100 per cent.

5. Double Permanent Total (D. P. T.)—any combination of those disabilities which entitle the beneficiary to an award for permanent total disability.

COMPENSATION FOR CARDIOVASCULAR DISEASE

Table XXI shows the number of veterans who are at the present time receiving compensation for cardiovascular disease incurred while in the military service together with the specific disease for which compensated.

In reviewing Table XXI it is noted that 16,189 beneficiaries are receiving compensation for cardiovascular disease as of March 31, 1927. The total compensable load consists of 239,433 beneficiaries. The per cent of the cardiovascular cases to the total is therefore 6.76.

The average monthly compensation of the cardiovascular cases varies from a low of $10.00 to a high of $110.00; the average for the whole group of 16,189 cases is $35.59 a month, as compared with the average monthly compensation for all beneficiaries, which is $44.55.

The annual outlay of the government for compensation for cardiovascular disease is $6,914,880.00; the total annual cost to the government for compensation for all disabilities is $127,993,800.00. The outlay for compensation for cardiovascular diseases is therefore 5.4 per cent of the total amount expended annually for the compensation of all classes of disabilities.

It is also noted in Table XXI that 5,822, or 35.96 per cent, of a total of 16,189 beneficiaries receiving compensation for cardiovascular disease are reported to have mitral insufficiency. It is believed that the incidence of mitral insufficiency in the Veterans Bureau is too high, and it is thought that the cause for it is the use of erroneous criteria in the diagnosis of this heart lesion. The mere presence of a systolic murmur at the apex does not mean mitral insufficiency. It is therefore possible that a number of the beneficiaries with this diagnosis are really cases of so-called functional heart disease. While it is probable that these patients have an occupational handicap, it is thought that, as a result of a favorable prognosis, physical and economic rehabilitation are possible.

Further study of Table XXI shows the principal cardiovascular diseases for which the disabled ex-service men are receiving compensation. The largest groups are, in the order named: mitral insufficiency, chronic myocarditis, neurocirculatory asthenia, aortic and mitral disease, mitral stenosis, aortic insufficiency, tachycardia, cardiac hypertrophy, chronic phlebitis, chronic endocarditis, hypertension, and aortic stenosis.

Table XXII is so arranged as to show the extent of disability for cardiovascular disease, the degree of handicap on a percentage basis, the number of beneficiaries within each per cent group, the average monthly payment, and the annual outlay for compensation for each group.

It is noted that 8,661, or 53.50 per cent, of the total of 16,189 beneficiaries are being compensated on a temporary partial basis. The compensation status of these men is of a temporary nature and may be changed after any physical examination conducted by the Veterans Bureau medical officers.

TABLE XXI

SHOWING THE NUMBER OF VETERANS RECEIVING COMPENSATION FOR CARDIOVASCULAR DISEASE, TOGETHER WITH SPECIFIC DIAGNOSIS, AVERAGE MONTHLY COMPENSATION AND TOTAL ANNUAL OUTLAY FOR COMPENSATION FOR EACH SPECIFIC DISEASE

CARDIOVASCULAR DISEASE	NUMBER OF BENEFICIARIES	AVERAGE MONTHLY COMPENSATION (DOLLARS)	TOTAL ANNUAL OUTLAY FOR COMPENSATION (DOLLARS)
Adherent pericardium	1	60.00	720.00
Aortic aneurysm	50	91.80	55,080.00
Angina pectoris	42	80.12	40,380.00
Aortitis	87	33.91	35,400.00
Arteriosclerosis, local	2	87.50	2,100.00
Arteriosclerosis, cerebral	56	74.29	49,920.00
Arteriosclerosis, general	114	84.69	115,860.00
Neurocirculatory asthenia	1,625	24.39	475,620.00
Auricular fibrillation	34	81.62	33 300.00
Bradycardia	9	22.22	2,400.00
Cardiac arrhythmia, extrasystole	48	31.56	18,180.00
Cardiac arrhythmia, sinus arrhythmia	21	24.76	6,240.00
Cardiac disorder, functional	2	35.00	840.00
Cardiac hypertrophy	476	29.91	170,820.00
Cardiac hypertrophy and dilatation	13	58.08	9,060.00
Cardiac murmur, not organic	20	16.75	4,020.00
Degeneration and infiltration of heart	3	53.33	1,920.00
Dilatation, aortic arch	8	56.25	5,400.00
Dilatation, cardiac, acute	3	75.00	2,700.00
Dilatation, cardiac, chronic	14	51.79	8,700.00
Embolism, cerebral	7	62.86	5,280.00
Endocarditis, acute	1	50.00	600.00
Endocarditis, chronic	348	35.63	148,800.00
Endocarditis, septic	1	55.00	660.00
Functional heart disease	12	26.67	3,840.00
Heart-block	5	110.00	6,600.00
Hemorrhage, cerebral	15	74.00	13 320.00
Hypertension	196	32.14	75,600.00
Hypotension	9	32.22	3,480.00
Mediastinopericarditis	1	40.00	480.00
Myocarditis, acute	3	58.33	2,100.00
Myocarditis, chronic	2,639	40.26	1,275,060.00
Pericarditis, acute, fibrinous	1	50.00	600.00
Pericarditis, adhesive	21	46.90	11,820.00
Pericarditis, purulent	5	61.67	2,220.00
Pericarditis with effusion	11	77.73	10,260.00
Phlebitis, chronic	434	26.18	136,320.00
Phlebitis, suppurative, chronic	4	15.00	720.00
Phlebosclerosis	1	100.00	1,200.00
Phlegmasia alba dolens	1	10.00	120.00
Pleuropericarditis	5	48.00	2,880.00
Tachycardia	490	20.62	121,260.00
Thrombophlebitis	99	31.77	37,740.00
Thrombosis	45	48.67	26,280.00
Valvular heart disease, aortic insufficiency	543	45.84	298,680.00
Valvular heart disease, aortic stenosis	148	49.36	87,660.00
Valvular heart disease, aortic and mitral	1,371	58.91	969.240.00
Valvular heart disease, mitral insufficiency	5,822	29.07	2,031,000.00
Valvular heart disease, mitral stenosis	1,314	37.87	597,120.00
Valvular heart disease, pulmonary lesion	8	26.88	2,580.00
Valvular heart disease, tricuspid lesion	3	75.00	2,700.00
Total	16,189	35.59	6,914,880.00
Grand total of active compensable beneficiaries	239,433	44.55	127,993,800.00

Per cent of total compensable beneficiaries receiving compensation for cardiovascular disease 6.76

Per cent of total annual outlay for compensation paid to beneficiaries for cardiovascular disease 5.40

Five thousand six hundred and forty-six, or 34.87 per cent, of the total number are on a permanent partial status. It was the opinion of the Veterans Bureau examiners that the cardiovascular disabilities of these cases were such as to constitute a permanent occupational handicap, but these men were not totally handicapped.

Seven hundred and seventy-eight, or 4.81 per cent, were placed on a temporary total compensation status. A great many of these beneficiaries were no doubt under hospitalization for the cardiovascular disease.

One thousand one hundred and four, or 6.82 per cent, of the total number of beneficiaries were on a permanent total status. In these cases it was thought by the Bureau physicians that the kind and character of the cardiovascular disabilities were such as to constitute a permanent total occupational handicap to the beneficiaries so grouped.

This, then, is the present cost to the United States of cardiovascular disease incurred by men and women who have been in the military service. A number of the beneficiaries with this class of disease have already died; an additional small number will be placed on the active compensation files of the Bureau from time to time after it is determined that their disabilities were incurred in or aggravated by military service in the World War.

TABLE XXII

SHOWING EXTENT OF DISABILITY, DEGREE OF IMPAIRMENT, AVERAGE MONTHLY COMPENSATION, AND THE ANNUAL COST OF COMPENSATION FOR 16,189 BENEFICIARIES WITH SERVICE-CONNECTED CARDIOVASCULAR DISEASE

EXTENT OF DISABILITY	DEGREE OF IMPAIRMENT (PER CENT)	NUMBER OF BENEFICIARIES	AVERAGE MONTHLY COMPENSATION (DOLLARS)	ANNUAL OUTLAY FOR COMPENSATION (DOLLARS)
Temporary Partial	10 – 19	2216	11.97	318,180.00
	20 – 29	2826	21.96	744,720.00
	30 – 39	1221	30.05	440,340.00
	40 – 49	692	38.23	317,460.00
	50 – 59	1072	47.35	609,120.00
	60 – 69	315	57.30	216,600.00
	70 – 79	281	68.83	232,080.00
	80 – 89	33	74.55	29,520.00
	90 – 99	5	87.00	5,220.00
	Total	8661	28.03	2,913,240.00
Permanent Partial	10 – 19	1871	12.65	284,100.00
	20 – 29	1931	22.69	525,720.00
	30 – 39	661	32.06	254,280.00
	40 – 49	347	41.31	172,020.00
	50 – 59	585	50.59	355,140.00
	60 – 69	121	61.86	89,820.00
	70 – 79	110	73.55	97,080.00
	80 – 89	19	83.16	18,960.00
	90 – 99	1	95.00	1,140.00
	Total	5646	26.54	1,798,260.00
Temporary Total		778	91.56	854,760.00
Permanent Total		1104	101.80	1,348,620.00
GRAND TOTAL		16189	35.59	6,914,880.00

The figures in Tables XXI and XXII stand out as excellent proof of the generosity of the people in providing amply for those who were disabled while in the service of their country.

SUMMARY AND CONCLUSIONS

1. a. There are 16,189 World War veterans at the present time with compensable cardiovascular disease. The living World War veterans number about 4,408,617. The incidence of this class of disease among the ex-service men is therefore approximately 3 per 1000. This is extremely low and the following reasons suggest themselves:

   1. The average age of the World War veteran is approximately thirty-six years, and heart disease morbidity and mortality begin to ascend after the age of forty.

   2. A large number of men with cardiovascular disease were kept out of the army by the draft boards, or, if accepted, were turned down at the various camps by the examining boards after it was ascertained that they had cardiovascular disease.

b. As the result of close contact in barracks during the war, infectious and contagious diseases were more prevalent among the military population than in civil life. This no doubt accounts for the high incidence of heart disease classified as the sequel of infectious diseases. This fact is one of the important observations in the study.

2. Of 736 Bureau patients under hospitalization for cardiovascular disease it was ascertained that there were a total number of 1123 lesions which were ascribed to 1761 etiological factors. It is supposed that the heart and blood vessels may be attacked by more than one disease, and each may leave an imprint of degenerative or inflammatory changes with resulting anatomical residua.

3. A consideration of the 1123 cardiovascular lesions found in 736 Bureau patients discloses the fact that the average number of lesions per patient is 1.53. The principal lesions are: mitral insufficiency, chronic fibrous myocarditis, hypertrophy of the heart, and aortic insufficiency.

4. a. In a study made of the specific cardiovascular lesions in a series of 736 Bureau patients it was noted that 453 had but one cardiovascular lesion; of the latter, the most common were mitral insufficiency, chronic myocarditis, and cardiac hypertrophy.

b. Two hundred and eighty-three patients had one principal and one associated cardiovascular lesion. The most frequent combination was mitral insufficiency with aortic insufficiency; the next most frequent combination was that of mitral insufficiency and hypertrophy of the heart; the next two most frequent combinations were those of mitral insufficiency and mitral stenosis, and cardiac hypertrophy and chronic myocarditis.

5. According to the etiological distribution of heart disease, 33.50 per cent of the cases were rheumatic; 30.04 per cent were sequelae of infectious diseases; 11.19 per cent were syphilitic; and 4.03 per cent were arteriosclerotic heart disease; the latter type is of interest in view of the fact that the average age of the living World War veteran is approximately thirty-six years.

6. A classification of 590 rheumatic factors according to the type of rheumatic infection causing heart lesions indicated that tonsillitis was the cause in 40.34 per cent of the heart lesions; acute rheumatic fever in 22.20 per cent; tooth and gum infections in 20.68 per cent; and the remaining rheumatic infections were such diseases as chorea, torticollis, pharyngitis, etc. These latter comprised 16.78 per cent of the total number of rheumatic infections.

7. In this study, heart lesions resulting from various infections diseases were classified as sequelae of infectious diseases. It is noted that influenza, pneumonia, and tuberculosis were the principal diseases reported as the cause of this type of heart disease. The most common heart lesions occurring as the sequelae of infectious diseases were mitral insufficiency, chronic myocarditis, and hypertrophy of the heart.

8. a. A study of rheumatic heart lesions disclosed the fact that in a considerable number of cases it was impossible to ascertain the time elapsing between the occurrence of the rheumatic infection and the appearance of the heart lesion. However, in those cases in which it was possible to obtain the information, it was found that the time varied from one month in patients in whom the heart lesion developed coincidently with the rheumatic infection to twenty-five years in patients in whom the lesion was not recognized clinically until that length of time after the occurrence of the rheumatic infection. In the majority of cases the lesion developed within five years.

b. In the case of syphilitic heart disease the statistics compiled show that luetic cardiovascular disease appears in the majority of cases from five to ten years after the initial infection.

c. What was said of rheumatic heart disease may be applied to heart disease, the sequel of infectious diseases. The time elapsing between the occurrence of the infectious disease and the appearance of the lesion varied from one month in cases in which the lesion appeared coincidently with the infectious disease to twenty-five years in patients in whom the lesion was not noted until that length of time after the occurrence of the infectious disease. In the majority of cases, clinical evidence of heart disease was observed within five years after the infection.

d. It is assumed that the interval of time elapsing between the occurrence of the etiological disease and the appearance of the cardiac lesion is dependent upon several factors, such as:

1. The type of causative disease

2. Extent of degenerative or inflammatory changes and location of lesion or lesions
3. Functional activity to which the heart is subjected

9. a. A study of the duration of cardiovascular disease in 736 patients in the Bureau hospitals showed that in 245 cases it was impossible to determine the duration of the heart disease. In the remaining number, namely 491 cases, heart disease existed for periods varying from one to six months in 30 cases, to eight to nine years in 41 cases. In 3 cases the heart disease was congenital. The largest group of patients, 85 in number, gave a history of having had the cardiovascular disease from seven to eight years.

b. In the consideration of 255 of a series of 736 patients who were hospitalized primarily for some heart lesion, it was found that the most common lesions present were chronic myocarditis, combined aortic and mitral valvular disease, mitral insufficiency, aortic insufficiency, and mitral stenosis. Taking the whole group of 255 cases into consideration, the duration of the various lesions extended from the shortest period of one to six months to the longest period of eight to nine years.

c. In a study made of the duration of various cardiovascular lesions in 252 Bureau beneficiaries who died from cardiovascular disease, the average period from the date of diagnosis of the lesion to the date of death was as follows:

For acute dilatation, eight months; acute endocarditis, four years; chronic endocarditis, four years; cerebral hemorrhage, two years; acute myocarditis, four years; combined aortic and mitral disease, five years; chronic myocarditis, four years; and mitral insufficiency, three years.

The duration of the various heart lesions just enumerated is shorter than is the usual experience.

d. Consideration of the duration of heart disease* is fraught with a good deal of difficulty because:

1. Exact date of the inception of the heart lesion is not always known.
2. Wide range in the duration period of various heart lesions.
3. Duration period depends upon etiological type of lesion, as well as upon the site of the lesion.

*It is thought that the figures of Romberg, showing that approximately fifteen years is the duration of the average case of heart disease should not be stressed too much, nor should the latter figure be applied in an empirical manner, inasmuch as heart disease is so varied as to etiology and clinical course as to make the period of duration also varied. It is believed that in considering the period of duration of heart disease, cases should be treated according to the etiological types to which they belong.

4. Duration period depends upon the reaction of the heart muscle to the lesion present, i.e., upon the rapidity of compensation or decompensation.

10. a. A study of the functional capacity of 736 cardiovascular patients, grouped according to the classification of the American Heart Association, shows that 28.40 per cent were able to carry on their habitual physical activity; 29.62 per cent were able to carry on a slightly diminished activity; 19.29 per cent were able to carry on only a greatly diminished activity; 11.14 per cent were unable to carry on any physical activity and were confined to bed; and in 11.55 per cent of the patients the functional capacity was not noted.

b. It is thus seen that 60.05 per cent of the patients had heart lesions which were accompanied by a reduced functional activity. From an economic standpoint this is a serious handicap inasmuch as the earning capacity of these patients is greatly impaired.

c. It follows, therefore, that the Bureau has the same problems to solve in the case of the cardiovascular patients as it had in dealing with the tuberculous beneficiaries:

1. To rehabilitate these patients physically.
2. To restore them to a maximum economic state.

d. It is thought that the Bureau facilities in the hospitals and regional offices could be utilized not only to restore these cardiac patients to normal heart function, but that they could also be used in the instruction of the cardiac patients in various light occupational crafts for the purpose of increasing their work tolerance. The Bureau, through outside social agencies, should interest itself in securing suitable occupations for the claimants after they are dehospitalized. These patients should be urged to return periodically for cardiac examinations so that the effect of work on the circulatory system may be determined.

11. In a series of 145 cases in which the cardiovascular disease was attributed to infected tonsils, and in which tonsillectomy was done, it was found that in 18 cases the cardiovascular disease was benefited by the operation. The small number of cases showing improvement is possibly due to the fact that in the others additional foci of infection were present, and that the extirpation of the tonsils did not rid these patients of all the areas of infection.

12. a. In a study of 60 patients who died while under hospitalization for cardiovascular disease, it was found that the average number of lesions per patient was 1.6; 29.31 per cent of the lesions were of rheumatic origin; 12.07 per cent syphilitic; 18.10 per cent were sequelae of infectious disease, and in 31.90 per cent of the lesions the etiological factor could not be ascertained.

b. Of the total number of lesions (100) in the above 60 patients, the largest groups were those of chronic myocarditis, enlargement of the heart, aortic insufficiency, mitral insufficiency, and mitral stenosis.

c. Of the 60 patients referred to, 32, or 53 per cent, died from organic disease of the heart; 4 from acute endocarditis, and 13 from pulmonary tuberculosis. It is noted that in a number of the patients, even though cardiovascular disease was present, it was not necessarily the primary cause of death, but might have been a contributory factor.

13. The statistics of the United States Veterans Bureau indicate that the mortality from cardiovascular disease between 1922 and 1926, inclusive, has increased from year to year with the exception of the year 1924, when there was a decrease in the number of deaths. This increasing mortality due to cardiovascular disease is to be expected as the ex-service man approaches the age of forty.

b. Of the 939 deaths due to cardiovascular disease and occurring between 1922 and 1926, 661 were due to organic disease of the heart.

c. The Bureau statistics show that 46.6 per cent of the deaths due to cardiovascular disease and occurring between 1922 and 1926, took place within the age group from thirty to thirty-nine, and the percentage of deaths in the succeeding age groups became less. This may be explained by the fact that the majority of the ex-service men are within the age group thirty to thirty-nine, and the number becomes smaller in the succeeding age groups.

d. An analysis of the 661 deaths due to organic disease of the heart reveals the fact that the principal primary causes of death were chronic myocarditis, mitral insufficiency, combined aortic and mitral lesions, and acute cardiac dilatation. It is also noted that 524, or 79.2 per cent, of the 661 deaths occurred before the age of forty, and 137, or 20.8 per cent, occurred after that age. This is different from the customary experience in civil life and may be explained by the fact that the average age of the ex-service man is thirty-six yars and the age at death of most of these men falls within the age groups up to forty years.

14. a. In a study of 1,845 deaths of insured Bureau beneficiaries due to cardiovascular disease, mitral insufficiency was the cause 498 times; acute cardiac dilatation, 324 times; cerebral hemorrhage, 302 times; chronic myocarditis, 216 times; acute endocarditis, 179 times; combined aortic and mitral disease, 122 times; acute myocarditis, 104 times; and chronic endocarditis, 100 times.

b. Two hundred and fifty-two of the 1,845 deaths were studied to ascertain the average age at death. It was found that of the patients with acute cardiac dilatation, the average age was thirty-four years; acute endocarditis, thirty-two years; chronic endocarditis, thirty

years; cerebral hemorrhage, thirty-seven years; acute myocarditis, thirty-two years; chronic myocarditis, thirty-three years; combined aortic and mitral disease, thirty-four years; and mitral insufficiency, thirty-five years.

15. a. The active compensable beneficiaries of the Bureau number 239,433 of which number 16,189, or 6.76 per cent, are receiving compensation for cardiovascular disease.

b. The average monthly compensation of the beneficiaries with cardiovascular disease is $35.59; the average monthly compensation of all beneficiaries is $44.55.

c. The annual outlay of the government for the compensation of beneficiaries with cardiovascular diseases is $6,914,880.00; the total annual cost to the government of compensation for all disabilities is $127,993,800.00; the outlay for compensation for cardiovascular disease is 5.4 per cent of the total amount expended annually for the compensation of all classes of disabilities.

16. Of the total of 16,189 beneficiaries receiving compensation for cardiovascular diseases, it is found that 35.96 per cent are reported to have mitral insufficiency; 10.04 per cent neurocirculatory asthenia; 16.30 per cent chronic myocarditis; 3.35 per cent aortic insufficiency; 0.91 per cent aortic stenosis; 8.47 per cent aortic and mitral disease; and 8.12 per cent mitral stenosis.

17. Of the total number of beneficiaries receiving compensation for cardiovascular disease (16,189), it is noted that 53.50 per cent are on a temporary partial basis; 34.87 per cent are on a permanent partial status; 4.81 per cent are on a temporary total status; and 6.82 per cent are on a permanent total status.

In conclusion it is desired to acknowledge the cooperation in this study of Dr. A. E. Cohn of the Rockefeller Institute for Medical Research, and a member of the Research Group of the Medical Council of the U. S. Veterans Bureau.

It is also desired to acknowledge the encouragement of the Medical Director of the U. S. Veterans Bureau in this study; and the cooperation of the Evaluation Division, Central Office, and of the medical officers in the field; the latter were kind enough to furnish the data which form the basis of this paper. The assistance rendered by Miss Anne Bambery, Statistical Assistant in the Research Subdivision, in the preparation of the manuscript is greatly appreciated.

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THE ELIMINATION FROM THE ELECTROCARDIOGRAM OF THE EFFECTS OF ALTERNATING CURRENT OF POWER AND LIGHTING LINES*

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During the last two years I have been attempting to determine the cause of waves in the electrocardiogram which correspond in rate to that of the alternating current of the electric lighting and power lines in the vicinity of the electrocardiograph. During the investigation certain information has been obtained which may be of use to others confronted with the same difficulty.

In attempting to locate the cause of alternating waves in the electrocardiogram, the first thing to do is to determine whether the offending current is picked up by the electrocardiograph, by the leads from the patient to the electrocardiograph, or by the patient himself. To do this it is only necessary to take three test photographs: (1) with the patient in the circuit; (2) with the patient removed and the leads joined together, and (3) with the leads removed and a short wire connecting the lead terminals of the resistance-box. If it is found that current is induced on the connecting leads, the latter should be covered with some metallic tube, such as lead pipe. When the electrocardiograph is situated some distance from the patient, certain precautions must be taken in the installation of the lead wires. Specific information on this can be obtained from the manufacturers of electrocardiographs, the main precautions as given by them being: (1) The leads should be enclosed in a metallic sheath, such as lead, and this sheath grounded every fifty feet. (2) As far as possible paralleling the alternating current lines must be avoided; if this is impossible, as it is in a great many instances, there should be a distance of at least five feet between them. (3) All alternating lines should be crossed at right angles and in this case a distance of not less than eighteen inches should be between them.

If it is found that the interference is picked up by the electrocardiograph, it may be that by simply shifting the position of the instrument in the room, the difficulty can be overcome. Wires concealed in the walls and floor are often found to be the source of trouble. If the currents are creeping up from the floor to the instrument or the patient, dry insulators should be placed under each leg of the table on which the electrocardiograph is mounted, and the chair or bed on

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which the patient is placed. Grounding both the resistance-box and the galvanometer to a water pipe should be tried. Leaving the galvanometer ungrounded and at the same time grounding the resistance-box and vice versa in some cases gives results.

Parts of the instrument may, under certain conditions, produce waves in the electrocardiograph simulating alternating current. If the camera motor is suspected, this may be eliminated by disconnecting it from the camera and taking a picture while spinning the latter by hand. When the source of light is any but that of an ordinary direct current incandescent lamp, the possibility of the trouble originating at this source should be ruled out. An ordinary six volt automobile headlight supplied with current from a storage cell of the same voltage will serve as a very easy method to check this part of the instrument. The time marker may be easily excluded by taking a tracing with it disconnected.

During the investigation it was found that if the ends of two leads were connected together by a coil of wire similar to the coils used as resistances in the resistance-box, the tracing showed marked alternating current effects and, in fact, the vibrations of the string could be easily seen with the naked eye. This led me to believe that possibly *currents were being induced in these coils during the taking of the* electrocardiogram, thus causing the disturbance. A complete resistance-box was constructed in which all coils of wire were substituted by noninductive carbon resistances; this, however, did not reduce the alternating effect in the tracings. A simpler method of excluding the resistance-box is simply to take a tracing with the patient in the circuit without the resistance-box; the shadow of the string will be forced to one side of the field of light, but it is quite possible to take a tracing in this manner, especially if the skin current of the patient is small.

The effect of accumulation of static charges on the galvanometer may lead one to think that they are the cause of foreign waves in the electrocardiogram; these charges are evidenced by the string periodically going into violent vibrations the amplitude of which ranges from zero in which the string can be sharply focused to a maximum when it cannot be seen; one complete cycle usually extends over a period of about four seconds and is immediately followed by another. Allowing this charge to escape, either by grounding or by the operator touching the galvanometer, usually stops the vibration. It was found that this effect may be present to the most marked degree and at the same time a perfect electrocardiogram be obtained.

When it is found that the effect of the lighting and power circuits is present only when the patient is connected to the leads, it would be well first to try placing a large piece of galvanized iron under the bed or chair. A piece of thick linoleum or other insulating material

the size of the metal sheet should cover it; the best results may be obtained by grounding the iron to the lead covering of the leads, and the lead covering in turn should be grounded to the resistance-box. If the above efforts fail, then the room in which the patient is placed should be lined with some metallic substance, such as "gravel screen," the lining being complete over the walls, ceiling, doors, and windows; the metal lining itself should be grounded. If the interference is not too great, placing a 4 M.F.D. condenser across the terminals of the string will give very good results and yet not modify the essential parts of the tracing to any great degree.[1] Valuable information on the protection of string galvanometer circuits against external electrical disturbances will be found in a paper by H. B. Williams.[2] If the electrical disturbance is of such a degree that none of the above measures eliminate from the tracing at all times the effects of alternating currents, it will be necessary to investigate the power and lighting lines in the vicinity of the instrument. In view of the fact that the electrocardiograph is disturbed only in certain localities, it occurred to me that the power lines in these districts must differ in some way from those in localities where there is no disturbance. It was found that the fault was not in the power and lighting lines themselves, but in certain motors, etc., receiving power from the same substation. These motors are supplied with 550 volts on a three phase system, which is not grounded. If a break occurs in the insulation of the windings of a motor, current passes from these windings into the frame and thus to the ground. This break in the insulation is evidenced at any point on the same line by a difference in potential between the other two phases and the ground. When first discovered, this difference of potential between one phase and the ground amounted to 540 volts. A recording voltmeter shows that the leak is not constant but varies from time to time, sometimes dropping to zero. Electrocardiograms taken when the voltmeter showed no leaks were free from alternating current effects, while those taken when the leak was large showed large waves corresponding in time to that of the local 25-cycle lighting and power circuit.

The solution of the problem is, therefore, in the repair or elimination of the offending electrical devices; these can best be traced out by the local electric lighting and power commission which will be glad to cooperate in the matter. It might be stated here that the first procedure is to conduct a thorough investigation in an attempt to locate the grounded machines and have them put in proper order or discarded; if it is impossible to find the trouble in this way, momentarily grounding the other phases will, for a time at least, remove the trouble and if often repeated will force the owner to discard the offending motor or other electrical device which is responsible for the leak.

SUMMARY

Information is presented which, it is believed, should prove of value in eliminating, from electrocardiograph tracings, the effects of disturbances from electric lighting and power circuits. The direct cause of the disturbance was found to consist in certain defective electric motors or similar devices receiving current from the same lines as the building in which the electrocardiograph is situated. The solution of the problem lies in the location and repair or elimination of the defective machines.

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Department of Clinical Reports

PLEURAL EFFUSION ASSOCIATED WITH CONGESTIVE HEART FAILURE LOCALIZED IN AN INTERLOBAR SPACE*

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STEWART† has recently reported pleural effusion associated with congestive heart failure, localized in an interlobar space. A rather careful survey of the literature reveals that the condition either is extremely rare or has not been reported. Hence the report of this case, which so closely parallels that of Stewart.

J. V. W., a male, fifty-one years old, traveling salesman, came under observation on May 28, 1928, complaining of dyspnea on the slightest exertion. Ten weeks before he had been recommended as a safe insurance risk by a competent examiner. A week later he noticed some difficulty in breathing. This had got steadily worse until on the day of examination, bending forward to tie his shoelace produced distinct shortness of breath.

The family history was unimportant and the past personal history negative. He had never had acute rheumatic fever, tonsillitis, chorea, or any of the streptococcic infections.

The present illness began nine weeks before he came for examination and was marked by constantly increasing dyspnea on exertion or haste, with slight cough, occasional spitting of blood, hoarseness, a sense of choking and gastrointestinal symptoms, especially the eructation of gas. He had had no previous medical attention.

The patient was an unusually robust man, 6 ft. 1 in. tall and weighed 235 pounds. There had been a loss of weight of ten pounds in the past eight weeks. He was markedly dyspneic on the slightest exertion. The skin was normally moist and there was no cyanosis. The frontal sinuses and antra transilluminated well. The pupils were regular and equal and reacted normally. There were several devitalized teeth. The tonsils had been removed. Examination revealed an enormously enlarged heart, but because of the thick chest wall it could not be definitely outlined by percussion. The heart sounds were remote and muffled and of a distinct tic-tac quality. There were no murmurs and no friction sounds. There were frequent premature contractions. The radial pulse rate was 108 with patient at complete rest. The systolic blood pressure was 180 mm. and the diastolic 120 mm. The breath sounds were not greatly altered except for scattered moist râles over the bases posteriorly. The liver was not enlarged, and there was no edema of the extremities. The prostate gland was normal.

An electrocardiogram showed an inverted T in the first and second leads and the QRS complex was slurred in all of the leads. There were frequent premature ventricular contractions. There was no axis deviation.

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†Stewart, Harold J.: Pleural Effusion Localized in an Interlobar Space, AM. HEART J. 4: 227, 1928.

The laboratory findings were as follows: *Blood:* Hemoglobin 87 per cent; red blood corpuscles 4,660,000; white blood corpuscles 6,700, with an increase in the polymorphonuclear neutrophiles to 83 per cent. *Urine:* Specific gravity 1.024 to 1.030; distinct trace of albumin; occasional finely granular casts and occasional pus cells. The nonprotein nitrogen was 60.6 mg. per 100 c.c. of blood and the uric acid was 4.6 mg. The Wassermann (blood) and Kahn tests were negative.

A flat plate of the chest taken at seven feet showed the heart enormously enlarged with the typical water bottle outline of pericardial effusion (no definite clinical signs of pericarditis were demonstrable). The cardiothoracic ratio was 75.7 per cent; the cardiac area (Bardeen) was 253 sq. cm. The striking finding in the

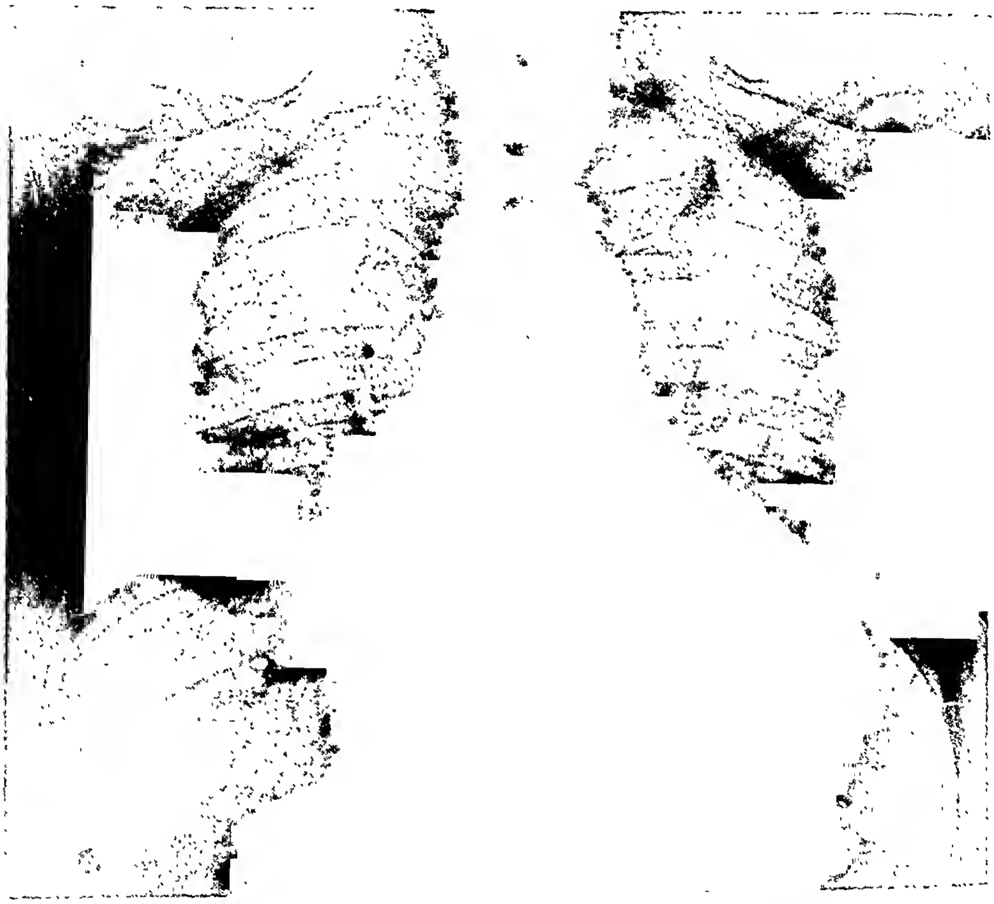

Fig. 1.—Localized pleural effusion and pericardial effusion.

roentgenogram was, however, a shadow seen in the right chest in the region of the interlobar space. (Fig. 1.) It was distinctly ovoid in shape and extended 8 cm. to the left of the right thoracic wall and was 5 cm. in width. The outline was perfectly regular and resembled, more than anything else, the shadow of a lemon. In density, the shadow was identical with that of the pericardial effusion.

The patient was put to bed and thoroughly digitalized. Clinical improvement was remarkably prompt and satisfactory. He stayed at rest for five weeks, but inasmuch as he was not in a hospital a further chest plate could not be obtained until July 12. (Fig. 2.) At that time the pericardial effusion had entirely disappeared, the cardiothoracic ratio had been reduced to 59 per cent, the area of the cardiac shadow was 198 sq. cm. (Bardeen) and the interlobar effusion had entirely disappeared. The cardiac rhythm was perfectly regular and compensation well

established. The blood pressure was 130/90 mm. No electrocardiogram was made.

The patient has continued to improve steadily and has resumed his former occupation. A seven foot plate made on January 5, 1929 was practically identical with that made on July 12, 1928, with no evidence whatsoever of the pleural effusion.

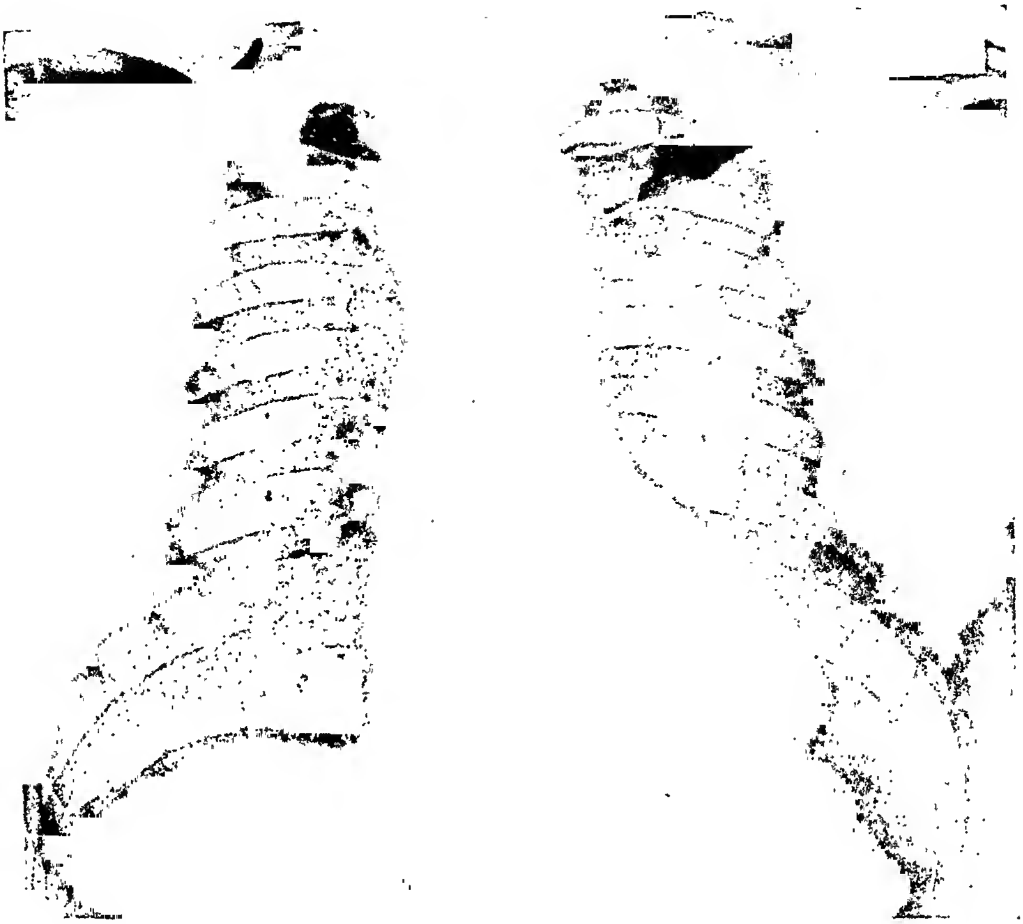

Fig. 2.—Note complete disappearance of both pleural and pericardial effusion.

The localization and character of the unusual shadow above described, together with its complete disappearance after the reestablishment of the cardiac compensation, the entire absence of any signs of neoplasm or empyema, justify, we think, the diagnosis of pleural effusion associated with congestive heart failure, localized in an interlobar space.

RETROPERITONEAL ABSCESS OF SPLENIC ORIGIN IN A CASE OF SUBACUTE BACTERIAL ENDOCARDITIS*

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THE following case is interesting because of the rare occurrence of suppurative processes following infarction of organs in subacute bacterial endocarditis and also because of the problem in diagnosis presented in such an instance.

J. K., a white woman, aged forty-two years, was admitted to the service of Dr. Hiram Loux of the Jefferson Hospital, July 19, 1928.

She complained of severe pain in the left upper quadrant of the abdomen. The family history was negative. The patient stated that she had been in good health until the onset of the present illness. She never had rheumatic fever, chorea, or tonsillitis. She had been pregnant eight times with normal labors. The present trouble began July 4, 1928, with severe pain in the left upper quadrant of the abdomen, fever, and urinary findings for which she was referred to the hospital with a note from the attending physician suggesting the diagnosis of pyelitis.

Cystoscopic examination revealed a normal bladder and normal ureteral orifices. Separate specimens of urine showed an insignificant number of white blood cells in each specimen. The patient seemed much improved after a week's rest and was discharged to a convalescent home on July 26, 1928.

Pain in the left upper quadrant recurred; she was readmitted to the hospital on September 4, 1928, and transferred to the medical ward on the service of Dr. Thomas McCrae, September 11, 1928.

Physical examination now showed a thin woman lying comfortably in bed. The mucous membranes were pale. The mouth and throat were in fair condition. The heart was enlarged to the left, almost to the anterior axillary line and a harsh blowing systolic murmur was heard at the apex. The pulmonary second sound was accentuated. The lungs were clear and resonant. The abdomen was distended, and the liver was enlarged to three fingers below the costal margin. There was a firm mass in the left upper quadrant of the abdomen which was tender at times. Neither physical nor roentgen-ray examination could establish that it was spleen, and yet it seemed continuous with splenic dullness. There was slight clubbing of the fingers. The temperature was very irregular with an occasional rise to 104°.

Urine examinations showed a trace to a cloud of albumin; a small number of pus cells, and occasional hyaline and granular casts, but no blood. Blood counts showed progressive secondary anemia with white blood cells varying between 6,000 and 10,000, the differential counts being unimportant. Numerous blood cultures were negative. Bacterial endocarditis was suspected, although it was felt that there might be additional trouble in the abdomen, such as perinephritic abscess. Pyelographic study of the left kidney showed apparently normal pelvis and calices, and additional roentgen-ray studies gave no evidence of perinephritic abscess. Nevertheless, the patient was operated upon October 10 under local anesthesia. A posterior incision exposed the left kidney but no abscess was found.

Roentgen-ray study on October 15 showed a mass in the left upper quadrant of the abdomen displacing the splenic flexure of the colon downward and inward.

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The lateral margin of the mass seemed to extend beyond the spine to the right, and the lower border was about the midpoint of the third lumbar vertebra. It seemed separate from the spleen which was somewhat enlarged.

On October 25 the blood culture showed a nonhemolytic streptococcus (not Streptococcus viridans) and this finding was confirmed on November 22. The patient never showed petechiae but shortly before death she complained of a very severe pain in the left wrist, and an area of bluish discoloration appeared on the ulnar side of the palmar surface extending into the palm of the hand. The temperature became very irregular with sharp peaks going to 104° and there were frequent sweats. Death occurred on December 7.

At autopsy (Dr. B. L. Crawford) the peritoneal cavity contained a slight excess of clear straw colored fluid. The abdominal organs occupied their usual positions. The spleen was enlarged and was densely adherent to the diaphragm and the lateral abdominal wall. There was a large retroperitoneal soft fluctuating mass on the left side of the abdomen which extended from the region of the spleen down to the brim of the pelvis. There was no evidence of inflammation of the general peritoneal cavity.

The heart was enlarged, weighing 420 grams; the muscle was soft and flabby. On the mitral valve and extending up on the wall of the auricle and down on the papillary muscles of the left ventricle were numerous long, pendulous, friable, reddish gray vegetations. Several were as much as 1¼ cm. in length. There was comparatively little thickening or deformity of the mitral valve leaflets. The aortic valve leaflets appeared normal. The coronary arteries were in good condition.

The spleen (430 grams) was enlarged and densely adherent to surrounding structures including the diaphragm, pancreas, and posterior abdominal wall. On releasing the adhesions a large pus pocket was found. This cavity was retroperitoneal and extended downward along the posterior abdominal wall to the brim of the pelvis. It contained about ½ liter of very thick greenish-yellow, foul-smelling pus. A large area of inflammation and necrosis was found in the diaphragm, and rupture had occurred into the left pleural cavity. The lung was adherent to the inflamed diaphragm.

There were several, circumscribed, soft grayish areas scattered throughout the spleen. On section some of these soft areas had partially necrotic centers and others had gone on to cavity formation. They had fibrous tissue walls and measured from 2 to 3 cm. in depth. Several of these reached the surface of the spleen and by rupturing, one such suppurative infarct must have been responsible for the retroperitoneal abscess.

The right kidney also contained a number of soft grayish infarcts.

Other organs did not show important changes.

Heart's blood culture yielded a nonhemolytic streptococcus and the same organism was recovered from the splenic abscess.

The significant findings therefore were: subacute bacterial endocarditis of the mitral orifice due to a nonhemolytic streptococcus (not viridans) and suppurative infarction of the spleen with retroperitoneal abscess formation and rupture of the left side of the diaphragm.

Department of Reviews and Abstracts

Selected Abstracts

Gladstone, Sidney A.: *A Few Observations on the Haemodynamics of the Normal Circulation; and the Changes Which Occur in Aortic Insufficiency.* Bull. Johns Hopkins Hosp. 44: 83, 1929.

The following paper presents a study of some of the phenomena associated with the physiology of a normal circulation and of the circulation as it is modified by various pathological processes in the light of principles of hydrodynamics.

The application of the hydrodynamic equation for the flow of water through pipes is made in an attempt to analyze certain problems in hemodynamics.

The forces concerned in cardiac contraction and the influence of respiratory movement are discussed. The fall of systolic pressure during inspiration is explained by the author as due to respiratory pressure changes in the mediastinum as the result of increased effort of respiratory movements. The change in blood pressure level during inspiration is just about equal to the changes of pressure which occur in the mediastinum during normal respiration.

Presents methods of calculating the work of the heart have underestimated the kinetic energy factor by failing to consider the systolic increase of velocity head imparted to the whole mass of arterial blood.

The general applicability of the principles of hydraulics to the problems of arterial flow is demonstrated by the author's ability to explain and correlate the findings of Dawson on the *Lateral Blood Pressures at Different Points of the Arterial Tree.* Brachial blood pressure is found to depend upon intra-aortic pressure head. Femoral blood pressure depends upon the sum of intra-aortic pressure head and velocity head, hence the so-called differential blood pressure.

The formation and propagation of the pulse are discussed. The present writer believes that the concepts of pressure waves have been applied erroneously in many problems of hemodynamics. For example, the nature of the pulse, the excess of femoral over brachial blood pressure, the difference between central and peripheral pulse, etc.

A well-developed case of aortic insufficiency is characterized by an exaggeration of the normal cyclic changes in pressure head, velocity head and total head of arterial blood. Evidence is offered for believing that the maximum velocity head especially increases above normal.

The present writer believes that the collapsing pulse is due to rapid egress of blood from the arterial system, resulting from the abnormally high systolic velocity head. A collapsing pulse diminishes the blood supply to the head and causes excessive mechanical strain of the arterial walls. An analysis is offered of the dynamics of regurgitation and the compensatory factors which tend to reduce the amount of blood regurgitation. The capillary pulse is believed to be a further consequence of the momentarily increased systolic velocity head and the exaggerated spurt-like character of arterial flood. The high femoral blood pressure in aortic insufficiency depends upon the high maximum velocity head of aortic and femoral blood. The brachial pressure may remain quite normal because the brachial and subclavian arteries arise at right angles from

the arch of the aorta and act as piezometer tubes, their flowing depending entirely upon pressure head and not being directly influenced by changes of intra-aortic velocity head.

The difference in mass of blood is only of secondary importance and may exaggerate the effect of water hammer. It is considered unnecessary to postulate an unequal distribution of pressure waves reflected from the periphery or even their existence in attempting to explain the excess of femoral over brachial blood pressure.

Gladstone, Sidney A.: Concerning the Mechanism of Production of the Korotkoff Sounds and Their Significance in Blood Pressure Determinations. Bull. Johns Hopkins Hosp. 44: 122, 1929.

The present writer offers an explanation of the method of production of the Korotkoff sounds based on an analysis of the various factors concerning their change during decompression of the cuff and their effect upon each other.

The sounds are produced by sudden distention of an artery, the walls of which were previously relaxed because the pressure of the surrounding pneumatic cuff opposes the diastolic intra-arterial pressure and keeps the artery undistended during diastole.

The appearance of the first sound is a measure not of systolic pressure head but rather of the sum of pressure head, velocity head and such increment as may be due to water hammer.

The dulling of the sound at the beginning of the fourth phase probably occurs just below the intra-arterial diastolic pressure head.

During the second phase the arterial sound weakens or disappears and is supplemented or replaced by a murmur. In such cases of hypertension or aortic stenosis, where the rate of arterial blood flow is not rapid enough to produce a murmur during the second phase, there is produced an auscultatory gap, since there is nothing to supplement or replace the arterial sound which during that phase weakens or disappears.

Lundy, Clayton J., and Woodruff, Lewis W.: Experimental Heart Block. Arch. Int. Med. 43: 184, 1929.

In the course of experimental work on the heart a new method was devised for increasing the intra-auricular and intraventricular pressures of the intact dog. This was done by tying a balloon on the tip of a properly bent glass rod and inserting the rod into the right auricle or ventricle by way of the right jugular and innominate veins. This apparatus was connected with a mercury manometer and a pressure bottle which permitted raising the intra-auricular pressure to any desired amount.

With an intra-auricular pressure of from 15 to 60 mm. of mercury, there was gradual lengthening of the P-R interval from 0.08 second to 0.2 second, a period of 2:1 block, establishment of an independent ventricular rhythm and finally complete suppression of the P-wave.

After release of the pressure in the balloon, there was a gradual return to the control type of sinus rhythm with normal P-R intervals.

Master, Arthur M., and Oppenheimer, Enid Tribe: A Simple Exercise Tolerance Test for Circulatory Efficiency With Stand Tables for Normal Individuals. Am. J. M. Sc. 177: 223, 1929.

The test here described utilizes habitual muscular movement causing a minimum of excitement and no dizziness or vertigo. It consists in ascending and

descending two steps, each 9 inches high. The number of foot pounds of work performed is easily calculated.

The advantages of a quantitative method for an exercise tolerance test are described, and its value in diagnosis is emphasized.

The criterion for the satisfactory performance of the test is a return of systolic blood pressure and of pulse rate to the pre-exercise level within two minutes after the end of exercise. Tables have been constructed giving foot pounds of work per minute performed by normal individuals with variation for sex, age, height and weight.

Curves of food pounds of work per minute plotted against age show that until about puberty girls perform more efficiently than boys, but after thirteen years males do better than females. The sharpest rise in the curve occurs between ten and twenty years of age. Males reach a maximum of about 3795 foot pounds of work at about twenty-six to twenty-nine years and women a maximum of 2950 at about twenty-four years. After this optimum of ages a gradual but steady decline occurs.

Exercise tolerance varies directly with body weight up to the optimum weight of 160 to 165 pounds for men and 135 to 145 pounds for women. Beyond these weights the exercise tolerance falls.

The relation of work capacity to height is a direct one, the taller the individual the greater is his exercise tolerance.

The practical importance of the procedure is that the patient can be tested to determine: first, whether his exercise tolerance is within normal limits; second, what his actual maximal tolerance is in foot pounds.

The test is helpful in the diagnosis and grading of circulatory efficiency and for tracing the changes arising therefrom during the progress of an organic condition of the heart or during recovery. It may also be used in giving advice as to sports and games.

Farrell, John T., Jr., Langan, Paul C., and Gordon, Burgess: A Roentgen Ray Study of a Group of Long-Distance Runners. Am. J. M. Sc. **177**: 324, 1929.

The present roentgenographic study was undertaken to determine the effect of long-distance running in 23 athletes. In a race from Los Angeles to New York these runners averaged 41 miles daily for 84 consecutive days. The study was made three days after the end of the race. They would indicate that when changes in the bones or sudden death are caused by athletic training or competition that the individuals were unqualified physically for strenuous effort, and exercise merely exerted a precipitating influence. In the teleroentgenograms the greatest transverse diameter of the heart was measured for comparison with the tables of Bardeen. The predicted diameter for each runner was computed for height and weight and an average obtained which was considered the normal diameter for the given individual.

The lungs were found to be essentially normal. The bones, except for certain osteoarthritis changes, were normal. The blood vessels were visualized only in the older runners.

In 13 runners the hearts appeared to be definitely smaller than normal; in 5 runners the hearts were within normal limits, and in five instances the hearts according to the predicted diameters showed an increase in size. According to the so-called cardiothoracic ratio, only one heart was increased in size.

The data as a whole suggest that the immediate effects of long distance running are inconsequential, since all the changes noted may be found in individuals of similar ages without symptoms.

Mond, Herman, and Oppenheimer, Enid Tribe: Gallop Rhythm in Hypertension. Arch. Int. Med. 43: 166, 1929.

In this paper the authors have attempted to elucidate the dynamic factors connected with the production of gallop rhythm by means of graphic methods giving exact records of the sounds and their relationship to the electrical and mechanical phenomena of the heart cycle. They have studied only patients presenting the classic syndrome of Potain, that is gallop rhythm in cases of hypertension with more or less marked cardiac insufficiency. By means of simultaneous electrocardiograms, phonocardiograms and apex impulse tracings, they have been able to ascertain the exact time relationships of the extra sounds to other events of the cardiac cycle and have considered which of such events may have a casual connection with the sound. They have found in agreement with all previous observations that in true gallop rhythm the extra sound occurs during ventricular diastole. The curves show that this extra sound on the phonocardiogram always occurs at the same time as the latter half of the P-wave and simultaneously with a large distinct wave of the apex beat and the A-wave of the venous pulse. This would, therefore, point to the auricular contraction as the determining factor.

As far as is shown by the records it would appear that the distinction between protodiastolic and presystolic gallop is not of great significance. Granting that in these cases gallop sound and auricular contraction are interrelated, it will depend entirely on the relative position of auricular contraction between the preceding second and the subsequent first sound whether the gallop is protodiastolic or presystolic. The factors determining this are, therefore, the rate of the heartbeat, on the one hand, and the length of the auriculoventricular conduction interval on the other.

They discuss the differentiation that must be made between gallop rhythm and the physiologic third sound and the reduplication of the second sound in mitral stenosis.

From their studies the authors believe that the mechanism of gallop rhythm is explained, as it was originally by Potain, as due to a sudden distention of the rigid fibrosed muscle wall of the ventricle by the inflowing blood from the auricle. In Potain's description, however, the rôle of the auricular contraction is neglected. The authors, however, believe that the auricle contracting plays an important part in the production of this sound. They proceed to discuss two questions: one, why is auricular contraction not heard under normal conditions; two, what are the conditions that make auricular systole an audible event? They believe that the auricle contracting is not heard naturally because there are factors causing the sound vibrations to be damped. Due to this fusion of the ventricular sound, the vibrations produced by the auricle contracting fall beyond the level of audibility. In the normal heart the ventricle is completely relaxed when auricular contraction occurs, its walls forming a soft, flexible mass which yields readily to the slightest pressure of the inflowing blood. In this phase auricle and ventricle form one large cavity, whereof the soft ventricular portion not only fails to participate in the vibrations of the auricle but also acts as a damper that silences whatever vibrations may have been started by the sudden contraction of the auricle muscle fibers. The amount of damping is clearly proportional to this yielding capacity of the normal ventricle muscle in diastole.

With rising tension of the ventricular wall the damping influence must be diminished and the chances of audibility improved. In the cases under dis-

cussion it is probable that factors are present in the ventricular muscle which make it favorable for the appearance of the sounds of auricular contraction.

The authors assume in explanation that the ventricular wall is no longer in a state of complete relaxation in diastole but now offers a marked resistance to the entrance of blood during auricular systole. The pressure wave produced by the contracting auricle meets with a ventricular wall which no longer yields passively to every impulse. The pressure is raised suddenly in the large common cavity comprising both auricle and ventricle, and the whole of its surrounding wall is thrown into transverse vibrations. These transmitted to the wall of the chest are heard as the familiar third sound of gallop rhythm. As has often been stated, it is best heard near the apex which is that portion of the vibrating muscle mass closest to the wall of the chest. In this conception the extra sound is a combined auricular and ventricular effect, and the participation of the ventricle explains why a sound, auricular in origin, should be so well perceived over the ventricle.

Symposium on the Aspects of Chronic Heart Disease. New England J. Med. 200: 1, 1929. 1: **Experience with Chronic Cardiac Patients at The Robert B. Brigham's Hospital.** Spear, Louis M.

The following points were emphasized as the result of this experience: (a) patients with endocarditis must be kept quiet as long as there is evidence of cardiac irritability; (b) there is a definite tendency to recurrence of cardiac infection under the best of control conditions; (c) the necessity for long rest in a hospital for the majority of cases, especially for those where home conditions are not suitable, to provide adequate rest; (d) the difficulty of control in cases that have been discharged to the Home Service is pointed out.

2: **Obtaining Occupation for Adult Males With Heart Disease.** Raymond, Howard C.

The usefulness of the classification of heart patients adopted by the New York Heart Committee has been proved in the placement of patients. It is pointed out that the doctor frequently may state what the patient cannot do, whereas the idea uppermost in the worker's mind is what he can do. Intimate relationship between the placement worker, the hospital social service worker and the employer is necessary. Various types of work suitable for male cardiac cases are enumerated.

3: **The Placement of Women With a Heart Handicap.** Fletcher, Gertrude L.

The author feels that the principles in placing women are the same as those in placing men. There is, however, one great advantage in placing women in the fact that many of the jobs calling for unskilled women are light, whereas those for unskilled men are heavy. On the other hand, there are many more places for unskilled men than for unskilled women.

4: **Home Adjustments in Chronic Heart Disease.** Upton, Nathalie B.

The adjustment of home problems stands out as one of the most challenging as well as one of the most hopeful problems presented. The author discusses the various phases in the home that require adjustment in order for the patient properly to meet his daily needs and life. How these home adjustments are to be made is a matter of technic which varies with the individual worker, the individual patient and the problem.

5: **Instruction in the Home for Children Handicapped by Heart Disease.** Terry Edith M.

The various questions arising in the care of young children with heart disease, as well as those during adolescent life, are presented. The need for supervision in school, in the home, in outside activities and preparation for vocational occupation are pointed out.

6: **Vocational Guidance for Children With Heart Disease.** Ginn, Susan J.

This particular phase of adapting children for future occupation is discussed. Interesting examples are cited where material benefit resulted to the patient from this phase of social work.

Heimann, H. L., Stracham, A. S., and Heyman, S. C.: Cardiac Disease Among South African Non-Europeans. Brit. Med. J. 344, Feb. 23, 1929.

The authors have analyzed the notes of all cases of heart disease among non-European patients of the Johannesburg General Hospital from March, 1924, to March, 1928. Although the cases are few in number, they serve as a useful guide for future investigation and represent one of the first reports of this disease among a native African population. The persons included in this study were those working in large towns and cities and therefore in contact with European population. Also they represent the more severe types of heart disase, since such people do not apply for admission until they are in the last stages of this disease. In all, there are notes on 153 cases of which 120 were Kaffirs, 31 were Eurafrican and 2 were Hottentots. Eighty-one died in the hospital. Approximately two-fifths of the patients were of rheumatic type. Of these 64 patients only about one-sixth gave a rheumatic history. There were 39 cases with syphilitic infection; 25 cases had degenerative lesions; 14 cases of bacterial endocarditis, and there were 8 persons with pericarditic lesions. The changes found at autopsy were similar to those described among European and American population.

The authors conclude from this study that there is very little divergence between the etiology, pathology and clinical signs of heart disease in Europeans and African non-Europeans.

Some important etiological factor in the causation of rheumatic fever might be elucidated by comparing the Kaffirs living altogether in the native state with the Kaffirs in the towns. The medical history of the Kaffirs before the influence of European civilization affected him is unfortunately not to be ascertained. The climate of South Africa, speaking generally, is one of sunshine and is hot and dry. It seems that climatic conditions as an etiological factor in the causation of rheumatism must be discountenanced here. Nasopharyngeal infections or bad teeth cannot be dismissed as factors, as they commonly occur in hospital patients. Their evidence in this series has not been determined. The dietary factor is a very variable one in the series. It is difficult to obtain exact knowledge but the Kaffir, as a rule, takes a diet of greater carbohydrate content and less fat and vitamine constituent than the European.

In regard to nonrheumatic cases little can be added to the facts already known.

White, Paul D., and Hahn, Richard G.: The Symptom of Sighing in Cardiovascular Diagnosis. Am. J. M. Sc. 177: 179, 1929.

The study of sighing has included observation and inquiry of its frequency in 650 cases mostly adults of whom 400 were normal controls, nearly all young men and women. One hundred were patients of organic heart disease who were

not especially nervous or tired. One hundred were patients of nervous fatigue or effort syndrome without heart disease, and 50 were patients with both organic heart disease and effort syndrome. Among the normal control persons sighing is a common finding but of frequent recurrence in only 19 persons. It was especially common as a frequent event in young women in the third decade of life, and it is generally recognized that it is this sex at this age that shows the greatest degree of nervous instability.

Frequent sighing is relatively rare in heart disease with or without congestive failure if there is no effort syndrome or marked nervousness.

In effort syndrome without heart disease excessive sighing is very frequent (80 per cent of 100 cases). When effort syndrome or marked nervousness is combined with organic heart disease, sighing is common. It is evident from the data that in these cases the sighing comes from the nervous state and not from heart disease.

Levy, Robert L., and Turner, Kenneth B.: Impaired Auriculoventricular Conduction in Rheumatic Fever. Arch. Int. Med. 43: 267, 1929.

In following a series of cases of rheumatic fever in which frequent electrocardiograms were made, the diagnostic importance of disturbances in auriculoventricular conduction became apparent. The records of all rheumatic patients in the course of nine years showing prolonged conduction or heart-block were critically analyzed in this study. For purposes of comparison all other cases showing disturbance in auriculoventricular conduction were similarly reviewed. A total of 145 cases was found. Of these 127 showed a prolonged P-R interval. More than one-half of these cases were instances of rheumatic fever. This prolongation of conduction time is by far the most frequent disturbance in this disease.

The authors have also studied the question of the involvement of the myocardium in cases of rheumatic fever. In their study they have found that of 403 patients, 112 (27.8 per cent) showed a long P-R interval.

A prolonged interval or heart-block occurring in a person under the age of thirty-five years who is not syphilitic and has not taken digitalis affords presumptive evidence of the presence of rheumatic carditis. This sign is often useful in establishing the rheumatic nature of a cardiac disturbance in the absence of other criteria. In 3 cases of acute tonsillitis, they found that there was definite prolongation of conduction time. They point out that in such cases there may be myocardial involvement of a rheumatic nature not recognized otherwise.

Prolongation of auriculoventricular conduction may persist and give evidence of myocardial lesions in rheumatic fever long after the other clinical manifestations of the disease have subsided.

Adams, S. Franklin: A Study of the Blood Pressure of Patients with Diabetes Mellitus. Am. J. M. Sc. 177: 195, 1929.

In this study the author has investigated 1001 diabetic patients in the Mayo Clinic. Arbitrary standards were chosen for high pressure and low pressure groups. The patient of any age was considered to have a high blood pressure if the systolic pressure was more than 150 mm. or if the diastolic pressure was more than 100 mm. In this group 16.2 per cent of the male diabetic patients, showed such an elevation of pressure and 26.7 per cent of the female diabetic patients had a similar elevation. The patient of any age was recorded as having low blood pressure if the systolic pressure was less than 110 mm. or the diastolic pressure was less than 70 mm. Of male diabetic patients 15.6 per cent had a systolic blood pressure lower

than 110 mm., and 19 per cent of diabetic women had systolic blood pressures less than 110 mm. These data like those of the high blood pressure group are averages for all ages. The final "weighted" averages of the group do not disclose any significant difference between the blood pressure of diabetic patients and that of normal persons.

The author concludes that there is no clear evidence that diabetes of itself promotes hypertension. If the blood pressure of diabetic patients is elevated, it suggests the presence of some associated abnormality which of itself is responsible for the hypertension.

Amberg, Samuel: Hypertension in the Young. Am. J. Dis. Child. 37: 335, 1929.

Twenty-five children with increased blood pressure and ranging from the age of six to sixteen years were examined and treated at the Mayo Clinic during the period of about eight years. A study of this group of cases forms the basis of this report.

The author divides the cases into the following groups: (1) hypertension associated with coarctation of the aorta; in these patients the elevation in blood pressure is confined to the upper part of the body, there is relatively low diastolic pressure, and there were pulsating superficial areas on the thorax; (2) hypertension as the consequence of an organic cerebral lesion; (3) hypertension perhaps in the form of so-called essential hypertension; (4) hypertension in the form of a syndrome of malignant hypertension, as described by Keith, Wegener and Kernohan with changes mainly in the small arteries and arterioles. These cases are characterized chiefly by persistent hypertension, absence of higher grades of anemia, adequate renal function at a time when striking lesions of the eyegrounds are visible and rapid fatal ending. The most important and constant feature is the extreme diffuseness of the histologic changes in the arteries and arterioles. These changes show a thickened muscular coat and hypertrophy of the lamina elastica which is split in places. (5) Hypertension associated with cardiac decompensation; (6) hypertension intimately associated with disease of the kidney. This whole group is not composed of homogeneous material, but no further attempt at a subdivision is made.

Eggleston, Cary: The Persistence of a Mitral Stenotic Murmur in the Presence of Auricular Fibrillation. Am. J. M. Sc. 177: 153, 1929.

It is the purpose of this communication to show that it is not uncommon to encounter patients with rheumatic mitral disease and fibrillation of the auricles in whom a mitral murmur is clearly heard to continue right up to the first sound of the heart. In a considerable portion of such cases this murmur sounds definitely crescendo at its termination in presystole and is, therefore, identical with that murmur which is regarded as most characteristic of mitral stenosis when the regular sinus rhythm is present.

The author believes that this apparent paradox is due to an auditory misinterpretation produced by the shortening of diastole and the accentuation of the first heart sound.

He states that two definite and distinct murmurs occur with stenosis of the mitral valve. The one is an isolated short murmur occurring synchronously with contraction of the auricles. It may be soft, blowing and rather indistinct, or, less commonly, it may be rough and rumbling. It usually gives the impression to the ear of being crescendo. This murmur is correctly attributed to the influence of auricular systole and should properly be called the auriculosystolic murmur.

The second murmur is not limited to presystole but begins at or before mid-diastole and continues through to end with the first sound in the heart. It is almost always coarse and rumbling, and it frequently seems to increase in intensity in presystole so that to the ear at least it appears to be clearly crescendo at its ending. This is the murmur which is most commonly present, and as in the case of auriculosystolic murmur it too is very commonly called a presystolic murmur. Since this murmur occupies a considerable portion of diastole and is never confined to presystole, it is much better to speak of it as the diastôlic murmur of mitral stenosis.

In the course of this investigation in a large number of patients who have mitral stenosis and auricular fibrillation, the author has never heard the isolated auriculosystolic murmur. The second type of murmur which begins at an earlier stage of diastole is the one which may remain after the auricles have passed into fibrillation. Its persistence has now been observed in more than 40 patients. All of the patients were suffering from rheumatic heart disease, and in all the evidences of mitral stenosis were such that this clinical diagnosis could not have been called into question. The presence of auricular fibrillation was established by electrocardiography. Several of the patients who died were proved at autopsy to have had advanced degrees of mitral stenosis.

The mechanism by which these murmurs are produced is that of the formation of a jet. Narrowing of the mitral orifice yields almost ideal conditions for the production of a rapidly flowing jet of blood as the stream enters the ventricle. When the stenosis is marked, the jet should occur throughout the greater part of ventricular diastole. In very pronounced stenosis it should persist until the intraventricular pressure begins to be raised to the level of that in the distended auricles by the onset of ventricular systole. Higher grades of stenosis are always accentuated by diastolic murmurs, and the duration of the murmur depends upon the degree of stenosis, the tighter the stenosis, the longer the murmur.

The author believes that the murmur under consideration never ends with a crescendo reinforcement in the presence of auricular fibrillation. The apparent crescendo ending is an auditory illusion due to the abrupt termination of the rough murmur by the loud sharply accentuated first sound which has the pitch that is not widely different from that of the murmur itself.

Palmer, Robert S., and White, Paul D.: The Clinical Significance of Cardiac Asthma. J. A. M. A. 92: 431, 1929.

In a group of 250 patients with cardiac asthma discovered in the past few years among 3100 private and hospital patients with organic heart disease, 180 were males, 70 females, and all except 14 were over forty years. The grave prognostic significance of the condition is shown by the fact that 170 of the 250 patients were known to have died with an average duration of life of 1.4 years after the first attack of cardiac asthma. The largest number of cases, 187, was found in a group of patients with coronary disease, hypertension, or both, but the highest relative incidence occurred in syphilitic heart disease and in chronic nephritis. Left ventricular failure due to any one or a combination of several factors appears responsible for cardiac asthma, but the exact mechanism is not clear. The frequency, duration and severity of the attacks alter the prognosis appreciably only when of an extreme degree. The coincidence of poor heart sounds, gallop rhythm and pulsus alternans indicated as a rule a very short life. Aortic regurgitation usually of syphilitic origin was the only common valve defect.

In therapy, digitalis and rest were generally effective in reducing the number of attacks and apparently prolonging life; for treatment of the acute attacks

nitrites and alcohol were sometimes helpful, while morphine was of the greatest value.

The mechanism of cardiac asthma as studied in this present group may be explained as follows. As a result of left ventricular strain and failure, with increased flood flow, a stasis of blood in the pulmonary circulation develops, the right ventricle sending on too much blood for the left ventricle to take care of. Gradually this accumulation of blood in the pulmonary circuit increases until by reflex stimulation the attack of asthmatic breathing is induced and the patient is awakened. By assuming the upright position, the stasis and also the strain on the left ventricle are reduced and recovery takes place.

White, Paul D., and Sprague, Howard B.: The Tetralogy of Fallot. J. A. M. A. 92: 787, 1929.

The tetralogy of Fallot consists of the most common grouping of congenital cardiac defects found in adults, namely, (1) pulmonic or infundibular stenosis; (2) interventricular septal defect; (3) dextroposition of the aorta, so that it overrides the septal defect and thus receives blood directly from the right as well as from the left ventricle; and (4) marked hypertrophy of the right ventricle. Clubbing of the fingers and cyanosis are invariably present.

The authors report the case of a notable musician, Henry F. Gilbert, who for nearly sixty years of his life suffered from congenital heart disease with cyanosis and clubbing of the fingers. The case is of interest first because he survived to his sixtieth year surpassing in age all patients previously reported by more than 23 years, and secondly and most significant because he made a great success of his crippled life, establishing himself in his musical profession as one of the greatest of American composers and as a pioneer of native American music. The history, accomplishments, physical examination, laboratory data and the conditions found post-mortem in this remarkable man are recounted.

The diagnosis of the cardiac defects was correctly made a year before his death. Fallot had demonstrated that this was possible forty years ago.

The authors report the case, believing that the account of this man's life may bring hope and inspiration to other victims of heart disease.

Richardson, Edward P., and White, Paul D.: Sympathectomy in the Treatment of Angina Pectoris. Am. J. M. Sc. 177: 161, 1929.

Eight patients with angina pectoris were operated upon at the Massachusetts General Hospital between August, 1923, and December, 1926. Since February, 1927, paravertebral injections of 85 per cent alcohol according to the method of Swetlow have been used instead of operation.

Among eight patients having eleven operations, there were two operative deaths. A lasting benefit followed operation in four cases and was directly attributable to it in three. On considering these results early in 1927 the authors were on the whole not greatly encouraged in continuing with sympathectomy of angina pectoris. As an alternative means of treatment it was decided to try the effects of paravertebral injection of alcohol.

Altogether eight patients have been treated by this means. These cases as a whole were comparable in seriousness to those treated by operation. The patients were either incapacitated or bedridden on account of the severity and frequency of their attacks. Three of them had coronary thrombosis and so would not have been suitable risks for operation; they survived the paravertebral alcohol injection without difficulty.

Symptomatic relief has more constantly been secured by paravertebral injections than by operation. While there was a tendency for pain to recur in

one or two cases, the relief generally lasted as long as the patients have been followed, up to eighteen months in one case.

The authors believe that treatment is justifiable in carefully selected patients who do not respond to other forms of treatment. They summarize the selection of cases as follows: paravertebral alcohol injection, generally of the left upper five thoracic nerve roots may be recommended in the treatment of obstinate angina pectoris which persists in spite of ample medical measures and which renders work impossible and life miserable. With these *indications there seem* to be no contraindications. The injections may be made even after coronary thrombosis and doubtless are much less risk than is cervical sympathectomy. It is quite possible that failure of a paravertebral alcohol injection may justify operative procedures, but their experience to date would indicate that the therapy of first choice for angina pectoris when medical measures have failed is the injection method.

Gilbert, N. C., and Kerr, John Austin: Clinical Results in Treatment of Angina Pectoris With the Purine-Base Diuretics. J. A. M. A. 92: 201, 1929.

All the drugs of this series have been used for the relief of anginal pains with ambulatory patients in the out-patient clinic discharged from the medical wards of St. Luke's Hospital, Chicago, since 1917. The authors describe the detailed technic of observing patients and the methods of administering these drugs. Their results are summarized in tables and are based on a total of 86 patients. They believe that the purine-base diuretics are of very definite value to many patients suffering from angina pectoris and should at least be given a fair trial in such cases. One preparation may be of greater value than another preparation very similar chemically, and the exact choice will depend on the individual study of each patient.

The authors believe from the study of these patients that the phenomena of angina pectoris can best be explained by a blood flow in the coronary vessels inadequate to the needs of the heart muscle at the moment. The purine-base diuretics are drugs capable of producing increased coronary flow. Beneficial results could then be expected when an increased coronary flow was not precluded by advanced anatomic changes in the vessels.

Eddy, Nathan B., and Hatcher, Robert A.: The Seat of the Emetic Action of the Digitalis Bodies. J. Pharmacol. & Exper. Therap. 33: 295, 1928.

The present investigation shows that nicotine abolishes the emetic action of pure digitalis principles which are in common use and also that of many of the crude drugs of this group.

A severely toxic dose of nicotine may be administered to a cat every half hour during many hours, showing that the drug is eliminated rapidly, but the action of nicotine whereby it abolishes the emetic action of digitalis bodies persists for three hours or more.

Dresbach, Melvin, and Waddell, Kenneth C.: The Emetic Action of Digitalis Bodies and Strophanthidin in Cats With Denervated Hearts. J. Pharmacol. & Exper. Therap. 34: 43, 1928.

The authors have examined experimentally the hypothesis that the origin of vomitiug induced by digitalis bodies arises in the cardiac muscle by denervating the heart of the cat in survival and acute experimetns.

It was shown that with the heart thoroughly denervated in survival experiments digitalis bodies or strophanthidin or both induce emesis with certainty.

It was further shown in acute experiments and in which the time for recovery from operative effects was greatly reduced that the animals failed to vomit in the greater number of cases. The conditions of the experiments in these cases strongly suggest, in the light of those of the longer method, that it is not safe to use the shorter method in the attempt to locate the seat of action in digitalis emesis.

The conclusion drawn is that in experimental animals, the heart cannot be said to be the sole seat of action of digitalis emesis; whether or not the same thing may be true of this emesis in intact animals is not yet known with certainty.

The possibility of strophanthidin acting on the peritoneum, as well as on the heart, to induce emesis is examined and seen to be not well founded, though such a possibility has not been disproved.

Bond, W. R., and Gray, E. W.: The Supposed Influence of Polarized Light on the Deterioration of Digitalis. J. Pharmacol. & Exper. Therap. 32: 351, 1928.

Studies have been made in connection with the deterioration of digitalis with age, particular attention being paid to the conditions under which the preparations have been stored. In view of the fact that certain tinctures exposed to daylight and artificial light for a period of time ranging from one to five years did not show any appreciable change in toxicity when assayed by the cat method and with the support of experimental evidence on tinctures radiated with polarized light of considerable intensity, the authors believe that the potency of digitalis preparations, as judged by the cat method of assay, is not lowered by exposure either to ordinary or to polarized light.

Gold, Harry, and DeGraff, Arthur C.: Studies on Digitalis in Ambulatory Cardiac Patients. II. The Elimination of Digitalis in Man. J. Clin. Investigation 6: 613, 1929.

The authors have been studying the various phases of the question of the elimination of digitalis and the duration of its effects in man. The studies have been carried out upon ambulatory cardiac patients with auricular fibrillation because in these the onset and disappearance of digitalis effects could be established with greater precision. The ventricular rate was used to indicate the intensity of the digitalis action, and this was particularly satisfactory in that group of patients who are in this respect very sensitive to the drug, in whom marked changes in the ventricular rate occur readily when the drug is given or withheld.

Two assumptions form the basis of the present study: first, that if a given degree of depression of conduction has been produced by digitalis and this effect is not increased in intensity by the administration of a fixed daily dose for weeks or months and no toxic symptoms occur, the patient is capable of eliminating that dose; second, if a fixed daily dose of digitalis produces progressively increasing depression of conduction, that dose is greater than the patient is eliminating. Thirty-four satisfactory tests were carried out on a series of 23 patients.

The authors conclude that the daily excretion dose is a misconception and that the amount of digitalis eliminated in a day cannot be stated as a given quantity under all conditions but varies with the amount of the drug present in the body.

Parkinson, John, and Campbell, Maurice: The Quinidine Treatment of Auricular Fibrillation. Quart. J. Med. 22: 281, 1929.

The object of this study has been to assess the value of quinidine in the treatment of auricular fibrillation in hospital and private practice and to see what advantages it may possess. The authors have studied 20 patients with paroxysmal and 44 with established fibrillation in whom quinidine seemed more appropriate than digitalis. As they were selected as occasion rose during five years, it is obvious that only a small proportion were thought suitable for this treatment.

Nine out of 18 cases of paroxysmal fibrillation were much improved, the attacks being abolished or greatly reduced for as long as the patient was under observation. In one-fourth of the cases the advantage was only temporary, and in the remainder there was no improvement at all. Quinidine, therefore, is the best treatment for this type of fibrillation whenever the attacks are of such length or frequency as to justify continuous medication provided the patient is well enough in the intervals. Its use for this purpose is devoid of risk.

In selecting patients with established fibrillation as suitable for treatment with quinidine, attention was paid to the etiology, to the duration of fibrillation and to the clinical condition, especially to the size of the heart and the signs of failure. The results were best of all where there was no rheumatic valvular disease and no hyperthyroidism, for all those in whom the arrhythmia was the only evidence of heart disease still have normal rhythm after an average period of two years. In these 44 selected patients with established fibrillation, normal rhythm was restored in 30 (68 per cent). In 23 patients, more than half of all who were treated, normal rhythm not only was restored but also was still maintained after an average period of more than two years and in one patient after five years. Four of these patients had short temporary relapses which were readily brought to an end with quinidine. The other seven of the thirty successes kept well for an average period of eighteen months before they reverted to fibrillation. With two exceptions all patients were strikingly better for the return of normal rhythm. Some were much better than they had been previously when taking digitalis, and many are now living such active lives that it is difficult to think that they could have been equally well with digitalis treatment.

Severe toxic effects were seen in two patients. Embolism, which occurred in two others but left no permanent disability, was found no more frequently in quinidine than under digitalis treatment. One patient died suddenly while taking quinidine.

When fibrillation has been established for more than six months, when there is a large heart or gross congestive failure, or when there is active rheumatic or syphilitic infection, there is more danger in using quinidine and less chance of lasting success.

The onset of fibrillation in a patient enjoying good or even moderate health should be regarded as a medical emergency. Quinidine, if it is used at once, is generally a safe and effective remedy and normal rhythm may be maintained for years.

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THE VENTRICULAR RATE IN AURICULAR FIBRILLATION STUDIES WITH THE CARDIOTACHOMETER*

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Auricular fibrillation is characterized clinically by a rapid, completely irregular, ventricular rate. The accepted explanation of this irregular tachycardia is that the auriculoventricular node and the bundle of His, owing to their refractory period, are unable to transmit the impulses of all the many fibrillary contractions of the auricles which are taking place at a rate of about 450 a minute. In the untreated patient from 100 to 200 auricular impulses a minute reach the ventricles effectively at irregular intervals and initiate ventricular contractions. When a patient with auricular fibrillation is treated with digitalis, a block in the conducting tissue that joins auricles and ventricles is produced which prevents the passage of most of the auricular impulses. In practical therapeutics the ventricular rate is thus reduced to 70 or 80. Excessive doses of digitalis may, however, lead to complete heart-block and idioventricular rhythms of from 30 to 40.

The action of digitalis is twofold: it increases the activity of the vagus inhibitory center, and it acts directly on the conducting tissue, in both ways causing diminished conduction or block. Other methods of stimulating the vagus in patients with auricular fibrillation, such as the administration of physostigmine[1] or pressure on the vagus in the neck or pressure on the eyeball, may also result in a slowing of the ventricular rate. Indeed, Sir Thomas Lewis has said: "If we examine all the known ways of reducing the ventricular rate while the auricles fibrillate, we find that heart-block may always be ascribed as the cause. The same cause alone reduces the ventricular rate in clinical cases."[2]

It would seem on superficial reflection that the ventricular rate of a patient with auricular fibrillation who had been thoroughly digitalized and in whom, therefore, a digitalis block had been produced would be fairly constant, that it would not markedly accelerate or

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retard in response to various extraneous stimuli. But as a matter of fact the ventricular rate of many patients with auricular fibrillation is variable from moment to moment, and this is the subject of the present study.

The rate and rhythm of the normal heart are determined by the sino-auricular node, the well-known pacemaker of the heart, which in turn is governed by the activity of the accelerator and the vagus nerves. When the auricles fibrillate, the sinus node no longer functions, and its chronotropic regulation by the extrinsic nerves of the heart is no longer possible. These nerves now affect the ventricular rate by altering the degree of block in the conducting tissue between auricle and ventricle, and this they do in a degree far greater than is generally recognized. Indeed, so well-informed a man as de Boer[3] has stated that when the auricles fibrillate the nervous regulation of the heart by the vagus and accelerantes is lost for the most part.

Mackenzie[4] recognized the great variability and lability of ventricular rate in patients with auricular fibrillation and believed that this was due to loss of control by the cardiac nerves. He described the great increase in ventricular rate following exercise and noted that after adequate digitalis dosage this reaction could be greatly diminished. He also described patients who at first need digitalis to maintain a slow ventricular rate, but who after a time do very well without digitalis. In these cases he believed the auriculoventricular node had become less excitable.

That vagus stimulation slows the ventricles during auricular fibrillation was demonstrated in animals as early as 1905[5] and many times subsequently, as well as that cutting the vagi of dogs with auricular fibrillation increases the ventricular rate.[6] That the vagus controls the ventricular rate in patients with auricular fibrillation has been shown by Robinson,[7] and by Fahrenkamp,[8] Weil[9] and Semerau[10] who found definite slowing following pressure on the vagus in the neck in 79 per cent of cases of auricular fibrillation. They claim that patients with heart failure and rapid ventricular rates react more often than those who are compensated and whose ventricular rate is slow. There seems to be a parallelism between reactivity to vagus pressure and to digitalis. It is said that hearts which slow under vagus pressure, slow more readily under digitalis medication than do those that do not show the vagus effect.

Kilgore[11] reported cases of auricular fibrillation with a periodic acceleration and retardation of ventricular rate apparently synchronous with the respiratory movements. He attributed the effect to fluctuations of conductivity of the bundle of His determined by the vagus.

Although many have noted an increased ventricular rate after exercise in patients with auricular fibrillation, the most careful study has been made by Blumgart.[12] He found that as compared to the normal

heart the heart with fibrillating auricles responds to exercise by a disproportionate rise in ventricular rate and by a delayed return to the previous resting rate. The same patients were retested after the heart's mechanism had been returned to normal by the administration of quinidine, and a similar reaction was observed. He concludes, therefore, that this exaggerated reaction is due not to the auricular fibrillation but to an additional factor. This factor may well be a valvular lesion or myocardial weakness. I have observed similar reactions in patients with mitral stenosis and regular rhythm. Blumgart found that tincture of digitalis in doses of 30 minims a day did not protect the ventricles from this exaggerated response to exercise. The resting heart rates of his digitalized patients were 76 or over except in two instances in which the rates were 58 and 68. Even in these cases he observed rises of ventricular rate of 67 and 62 respectively after exercise. Mackenzie[13] on the other hand claims that if adequate doses of digitalis are given this exaggerated response of the ventricles to effort can be controlled. Lundsgaard[14] has made similar observations.

Gallavardin[15] has described patients with auricular fibrillation with ventricular rates of from 35 to 50 due to partial heart-block and attacks of syncope, who showed an increase in ventricular rate (in one case from 40 to 117) following exercise.

The acceleration of ventricular rate in patients with auricular fibrillation following the administration of atropine has long been known.[16]

In auricular flutter the ventricles react as a rule to every second, third or fourth auricular beat. Vagus stimulation or digitalis slows the ventricles by producing a partial heart-block, exercise and excitement exert the reverse effect.[17]

It is evident from these many observations that even when the auricles fibrillate or flutter the ventricular rate is under control of the extrinsic nerves of the heart. The significance of this in the clinic, however, is not fully appreciated.

I have studied the ventricular rate in a group of patients with auricular fibrillation and auricular flutter by means of my cardiotachometer.[18] This is an instrument which counts the ventricular rate automatically over long periods of time while the subject is pursuing his ordinary physical activities. Registration is not disturbed by exercise. The action current of the heart is led from the chest by special electrodes through wires from 60 to 100 feet long to a specially constructed radio amplifier which amplifies it some 6000 times. The amplified current operates a relay system which in turn operates an electromagnetic counter which counts the heartbeats. In addition a pen writing on a moving tape records every beat of the heart. Patients were kept under observation from fourteen to twenty-four hours.

Figs. 1 and 2 represent twenty-four-hour records of the ventricular rate in a girl fourteen years old with mitral stenosis and auricular fibrillation; Fig. 1 undigitalized, Fig. 2 after 23 c.c. of tincture of digitalis had been administered in the preceding ten days. The patient was in bed unless it is otherwise noted. The great lability of the heart rate is apparent in both records. The range of variability is if any-

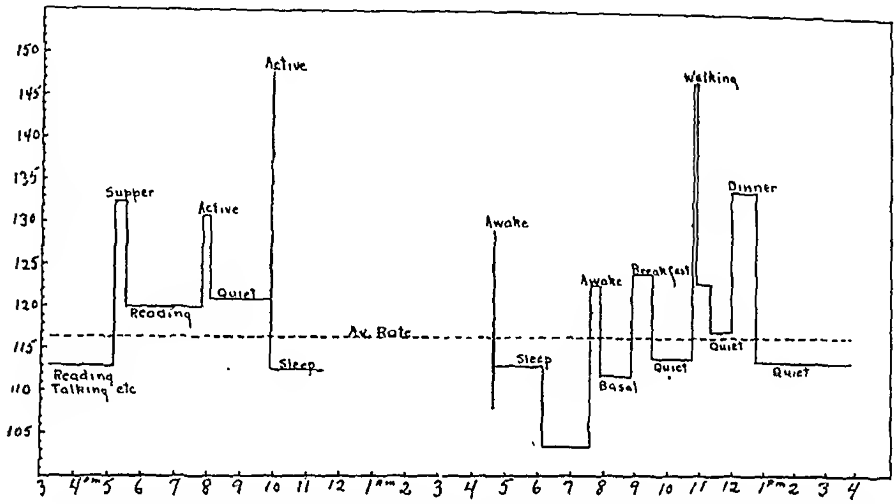

Fig. 1.—Auricular fibrillation; undigitalized. Total time 19 hours, 36 minutes. Total heartbeats 137,101.

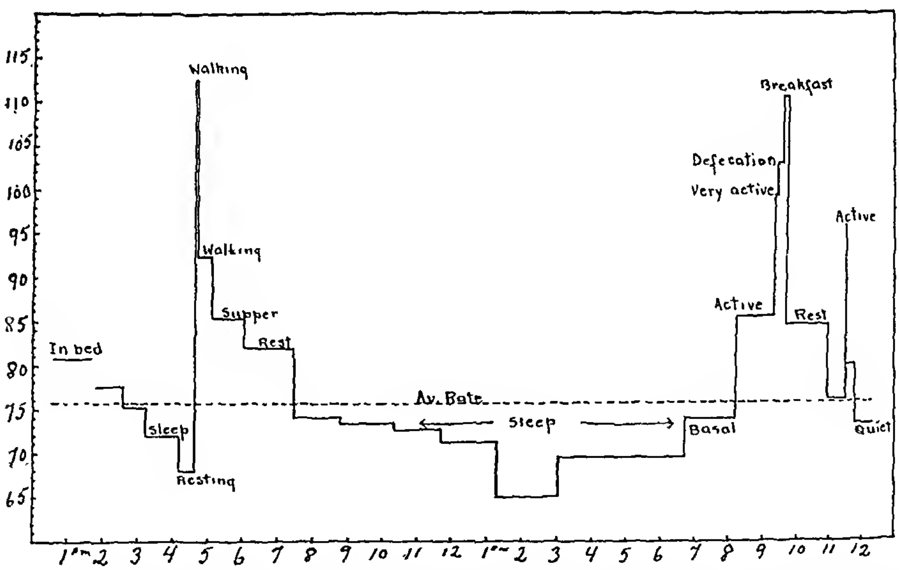

Fig. 2.—Auricular fibrillation; digitalized. Total time 23 hours, 33 minutes. Total heartbeats 107,291.

thing greater when the patient is under the influence of digitalis but takes place at a lower level. It is striking to see how relatively slight activity, such as that involved in eating, will accelerate the ventricles from 15 to 20 beats. Walking provokes an increase in rate of from 33 to 46 beats a minute. Sleep on the other hand slows the ventricular rate, the drop being most marked after several hours of sleep. Fig. 3,

representing very frequent readings in a man with auricular fibrillation who was under the influence of digitalis, shows these constant variations in ventricular rate still more clearly. A simple conversation suffices to produce an acceleration of 18 beats; walking provokes a rise of 73 beats; eating provokes a rise of 8 beats a minute; and a short nap reduces the rate by 16 beats a minute.

These charts demonstrate very clearly that if the generally accepted explanation of the mechanism of ventricular activity in auricular fibrillation is correct—and there is every reason to suppose that it is—the frequency of ventricular contraction is under control of the vagus and accelerator nerves. The activity of these nerves is con-

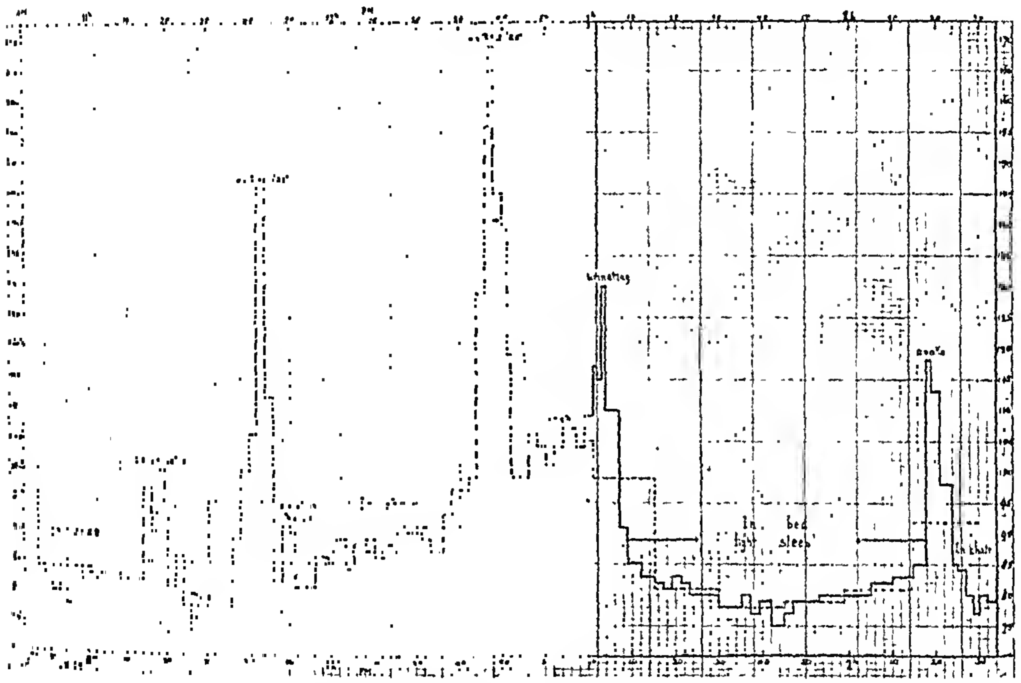

Fig. 3.—Auricular fibrillation. Variability in rate. ——— readings every few minutes; - - - - readings every 15 minutes.

stantly manifest by changes in rate in response to manifold stimuli, just as in normal sinus rhythm. Their mode of action in auricular fibrillation is different, however, for instead of regulating the speed of impulse formation in the sino-auricular node, they act by altering the refractory period or the conductivity of the auriculoventricular node and the bundle of His. In view of the fact that both vagus and sympathetic inosculate around the auriculoventricular node, as well as around the sinus node, this phenomenon is quite comprehensible.

Individuals with normal sinus rhythm show widely varying degrees of lability of heart rate. In those who are phlegmatic the rate tends to be stable; in those who are high-strung, acceleration and retardation of the heart in response to the manifold stimuli of everyday life are excessive. A similar increased lability is seen in patients with

Graves' disease and during fevers as well as during convalescence from acute infectious diseases. Patients with auricular fibrillation vary similarly in the degree of lability of their ventricular rates. These different types of ventricular response depend not on the auricular fibrillation as such but on the activity of the extrinsic cardiac nerves. Their recognition is of the utmost importance in therapeutics, for successful treatment with digitalis predicates an understanding of the effect of neurogenic factors on ventricular rate.

Patients with auricular fibrillation have been grouped according to their ventricular rates. Semerau[9] in a study of 111 cases found 71 cases or 64 per cent with rapid rates, i.e., rates over 80, and 37 cases or 33 per cent with slow rates, i.e., under 80. About 10 per cent of the cases had ventricular rates under 60. This distinction was made by Mackenzie[19] in 1911, who noted that slow rates were found in older patients suffering from the degenerative forms of heart disease. In these patients, in his experience, the ventricles slowed but little under digitalis therapy. He attributed the infrequent ventricular beats to organic block in the conducting tissue. Later authors have largely followed his interpretation.[20]

But this explanation is not altogether satisfactory. Block in the auriculoventricular conducting tissue may be due to actual lesions involving the tract; it may be functional due to an increase in the number of auricular impulses showered upon it; it may be due to impaired nutrition; it may be determined by vagus action or by the effect of drugs, such as digitalis. On the other hand it has been shown experimentally that conduction may be improved by stimulation of the accelerator nerves and that in auricular fibrillation this leads to an increased number of ventricular beats.[21] Both Gerhardt[22] and Cushny[23] saw in this mechanism the explanation of the phenomenon that in patients with auricular fibrillation and a slow ventricular rate the rate becomes rapid when the heart becomes insufficient due to overexertion or infection. Exercise hastens the ventricular rate in the same way. This is quite analogous to the reaction to exercise noted in certain patients with complete heart-block in whom the block is temporarily lifted, due to the "work reflex" via the accelerans.[24]

It is evident that the varying ventricular rates encountered in patients with auricular fibrillation cannot for the most part be explained by assuming different degrees of heart-block on an anatomical basis. It seems clear from the evidence in the literature as well as from the lability of rate shown in my records that the activity of the extrinsic nerves of the heart must play a considerable rôle. Hoffman[25] is one of the few authors to emphasize this view. Robinson[20] points out that the cause of ventricular slowing following rest is unknown.

Indeed a number of facts demand explanation. Why is the ventricular rate usually very rapid at the first onset of auricular fibrilla-

tion, particularly when the fibrillation occurs in paroxysms; and why does the ventricular rate become slower when the disturbance of the auricular mechanism becomes permanently established? Why do certain of these patients at first exhibit rapid ventricular rates requiring continuous digitalis dosage and then after a period of such medication show ventricular rates below 80 long after digitalis has been discontinued? Why do these same patients after an intercurrent infection or physical overstrain revert to high ventricular rates and again require large amounts of digitalis? Why is the ventricular rate of patients with exophthalmic goiter and auricular fibrillation rapid, as a rule, even after digitalis medication? I have observed this a number

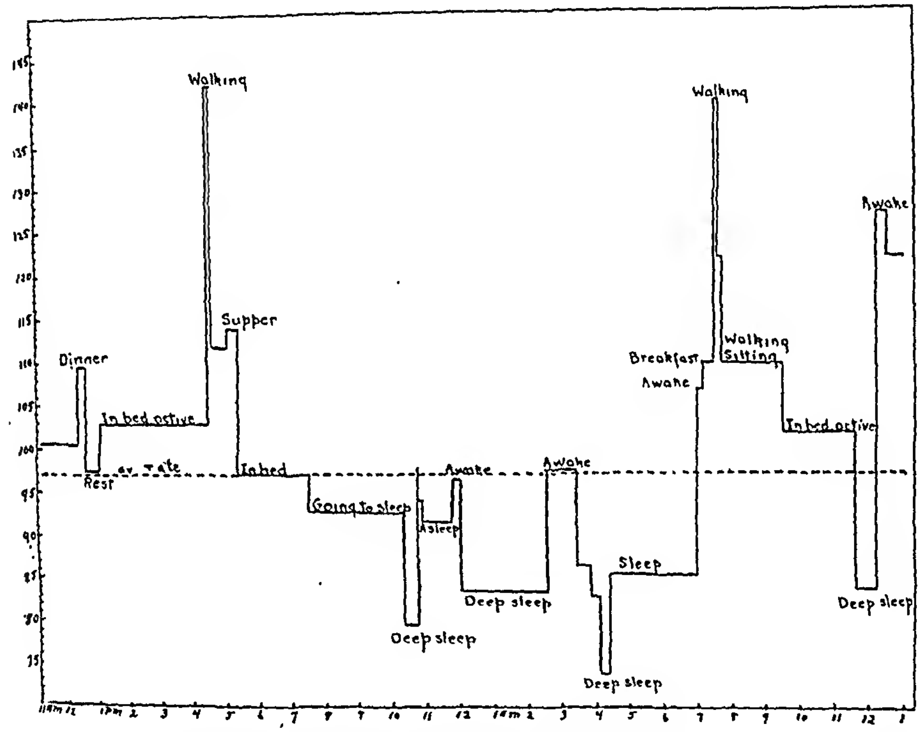

Fig. 4.—Auricular fibrillation; partly digitalized. Total time 25 hours, 49 minutes. Total heartbeats 150,304.

of times, and it is well shown in the case reports of Baumgartner, Webb, and Schoonmaker,[26] although they do not draw attention to it.

I believe that these phenomena can be explained on the basis of alteration of tone of the vagus and accelerator nerves. For instance, the sympathetic nervous system is hyperactive in exophthalmic goiter. This would increase the conductivity of the conducting tissue of the heart and so allow a more rapid ventricular rate. There is further evidence of the correctness of this view.

Patients with auricular fibrillation may be classed in two groups: those with a labile and those with a relatively stable ventricular rate. Individuals with labile ventricular rates are usually high-strung and nervous; they correspond to individuals with normal rhythm and

symptoms of neurocirculatory asthenia. Emotional surges and physical exertion provoke exaggerated rises in ventricular rate; rest and sleep are accompanied by low ventricular rates. This lability of ventricular response persists after thorough digitalization. Individuals with stable ventricular rates are, as a rule, calm and phlegmatic. The ventricular rate responds only to a moderate degree to emotion and exercise and is readily kept under control by digitalis.

Case 1, a young man with rheumatic mitral stenosis and aortic insufficiency, had a ventricular rate of about 200 when first seen. Pressure on the eyeball effected marked slowing of the ventricles and made possible the recognition of the absolute irregularity which was ob-

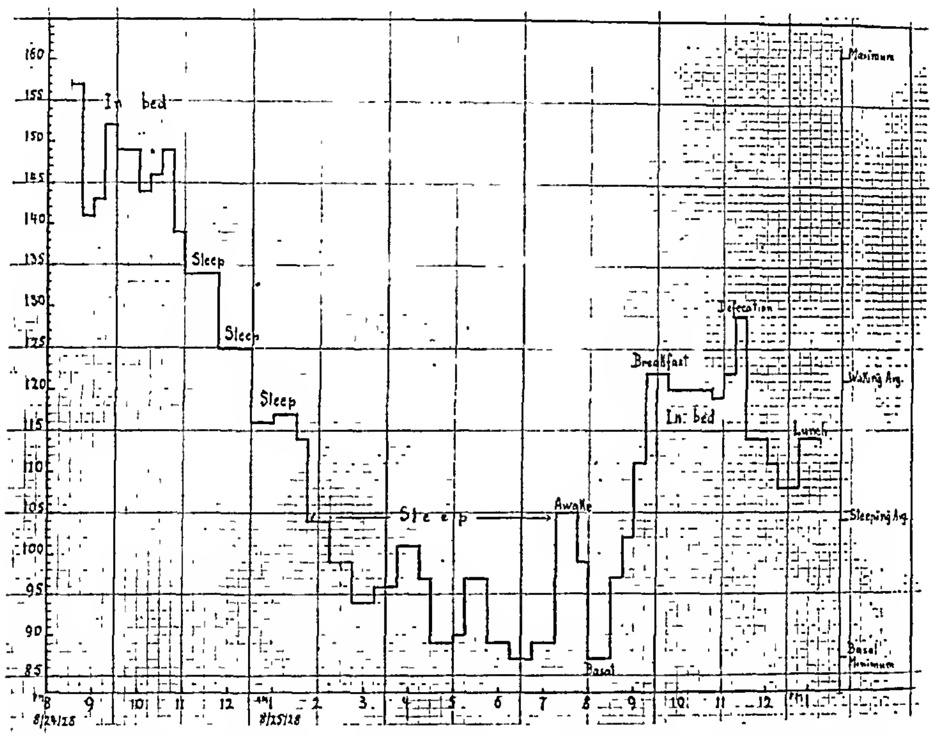

Fig. 5.—Auricular fibrillation; 75 c.c. tincture of digitalis, July 22-August 17, none since then. Total time 16 hours, 53 minutes. Total heartbeats 114,251.

secured by the rapid heart action. The patient was nervous and high-strung and had a marked anxiety neurosis. Although he received 3 c.c. of tincture of digitalis daily for several weeks, his ventricular rate remained rapid and very labile. His cardiotachometric record (Fig. 4) was taken after he had received 28 c.c. of tincture of digitalis in thirteen days following the previous dosage. The lability of ventricular rate, the exaggerated response to exercise, the marked drop during sleep are evident.

Cases 2 and 3 are similar in type: high-strung individuals whose ventricular rates were usually rapid during their waking hours, slowing to 85 and 76 during sleep. Case 2, a man thirty-seven years old, with rheumatic mitral stenosis and cardiac insufficiency, under heavy doses

of digitalis had a ventricular rate of 84, yet at other times in spite of even larger dosage the rate was 120. Several times a week he had paroxysmal attacks of rapid ventricular rate of from 150 to 160 accompanied by pain in the precordium and a sense of choking. The cardiotachometric record (Fig. 5) clearly illustrates the marked lability of ventricular rate and in particular the profound drop during sleep. This reduced ventricular rate during sleep is shown by all patients with auricular fibrillation and is analogous to the drop in rate observed in individuals with normal sinus rhythm. It is due apparently to the great diminution during sleep of physical and psychic stimuli which act reflexly on the heart. Subsequently this patient received much larger doses of digitalis—51 c.c. of the tincture in ten

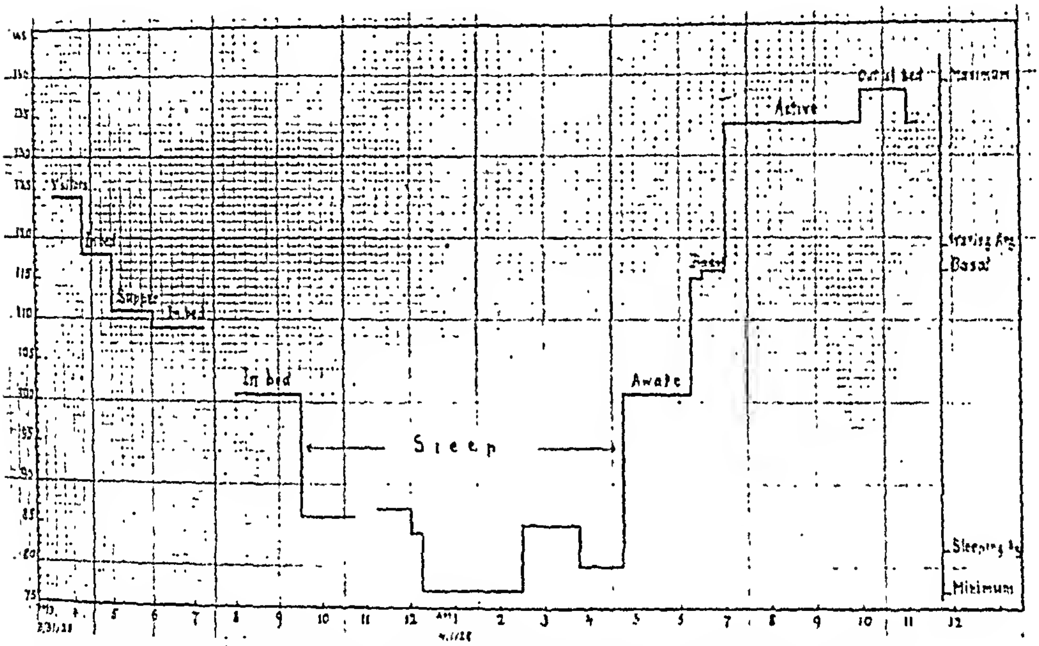

Fig. 6.—Auricular fibrillation, tincture of digitalis 33 c.c. from March 20-March 28. Total time 18 hours, 38 minutes. Total heartbeats 118,148.

days, or three times the body-weight dose. This kept his ventricular rate at about 86 even during his waking hours.

Case 3, a man with rheumatic mitral stenosis, aortic insufficiency, and auricular fibrillation had received 33 c.c. of the tincture of digitalis in eight days. The ventricular rate at rest was 85. The slightest excitement, such as that occasioned by the approach of a physician or a nurse, induced a rate in the neighborhood of 160, which dropped only gradually. He has a marked anxiety neurosis, and many of the symptoms of neurocirculatory asthenia. The periods of rapid ventricular rate are accompanied by flushing of the face. His curve (Fig. 6) shows the rapidity of his ventricles during the day and the marked drop during sleep.

Cases 4 and 5 show the contrast between the labile and the phlegmatic types to better advantage. They are two boys with rheumatic

valvular disease and auricular fibrillation, both thirteen years old. The first has mitral stenosis, and the second has mitral stenosis and aortic insufficiency.

In Case 4 (Fig. 7) without digitalis the ventricular rate ranged from 81 to 120 and was fairly steady. After small doses of digitalis, only 13 c.c. of the tincture spread over twenty-one days, the rate dropped considerably and became still more stable. On the other hand Case 5 (Fig. 8) when untreated had a ventricular rate which ranged from 98 to 167 and did not drop below 100 during sleep. After 24 c.c. of tincture of digitalis in seven days his ventricular rate showed a very satisfactory drop but not so low a range as that of the other boy.

It must be borne in mind that all these patients have hearts with other damage in addition to the auricular fibrillation. They have valvular disease and varying degrees of myocardial insufficiency. Such hearts even with normal rhythms show a marked lability of rate in

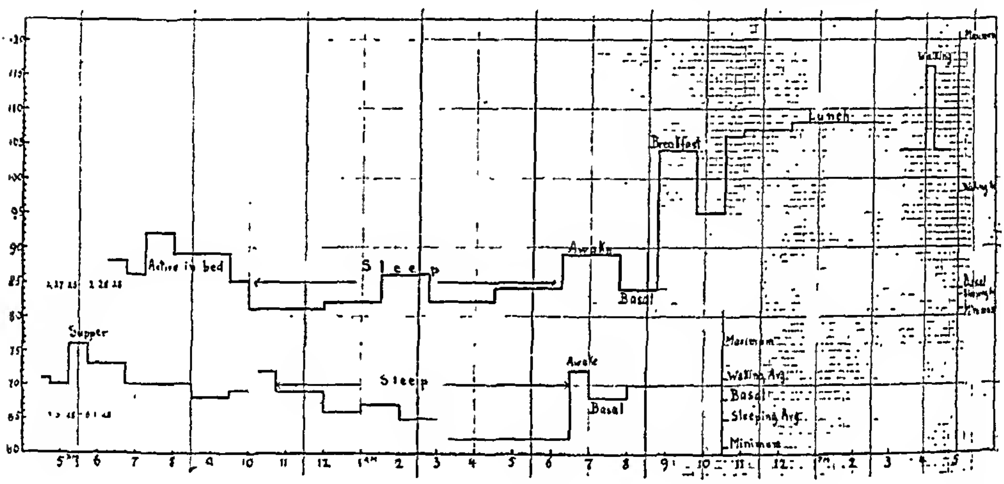

Fig. 7-*a*.—Auricular fibrillation; undigitalized. Total time 22 hours, 1 minute. Total heartbeats 121,362.

b.—Auricular fibrillation; digitalized. Tincture digitalis 10 c.c. from May 10-May 20. Tincture of digitalis 3 c.c. from May 26-May 31. Total time 16 hours, 22 minutes. Total heartbeats 66,670.

response to various stimuli. That this plays a rôle in the cases under discussion has been shown by Blumgart.[12] But even this effect must take place through the intermediation of the nervous system. Although the ventricles of hearts with fibrillating auricles are under control of the cardiac nerves and react by changes in rate to the many stimuli engendered by the bodily functions, this regulation is not so well adapted to fit the cardiac response to the circulatory needs of the body. There is overshooting; the reaction is often excessive.

All of the above observations lead to a number of interesting and practical conclusions. They illustrate again very clearly that the action of a drug depends just as much on the reaction of the individual subject as on the innate properties of the drug. The dosage of digitalis necessary to achieve a certain effect will depend as much upon

the vagus-accelerator tone as upon the body weight of the patient. Patients with different nervous constitutions react differently to identical doses of digitalis when their auricles are fibrillating. Those who are high-strung and anxious have rapid ventricular rates, and larger quantities of digitalis are required to slow the ventricles. The ventricular rate remains labile even after much digitalis has been administered and after the characteristic changes in the T-wave, indicative of digitalis action, have appeared. Individuals who are more phlegmatic tend to have slower ventricular rates which are readily retarded and stabilized by the usual doses of digitalis. The first group

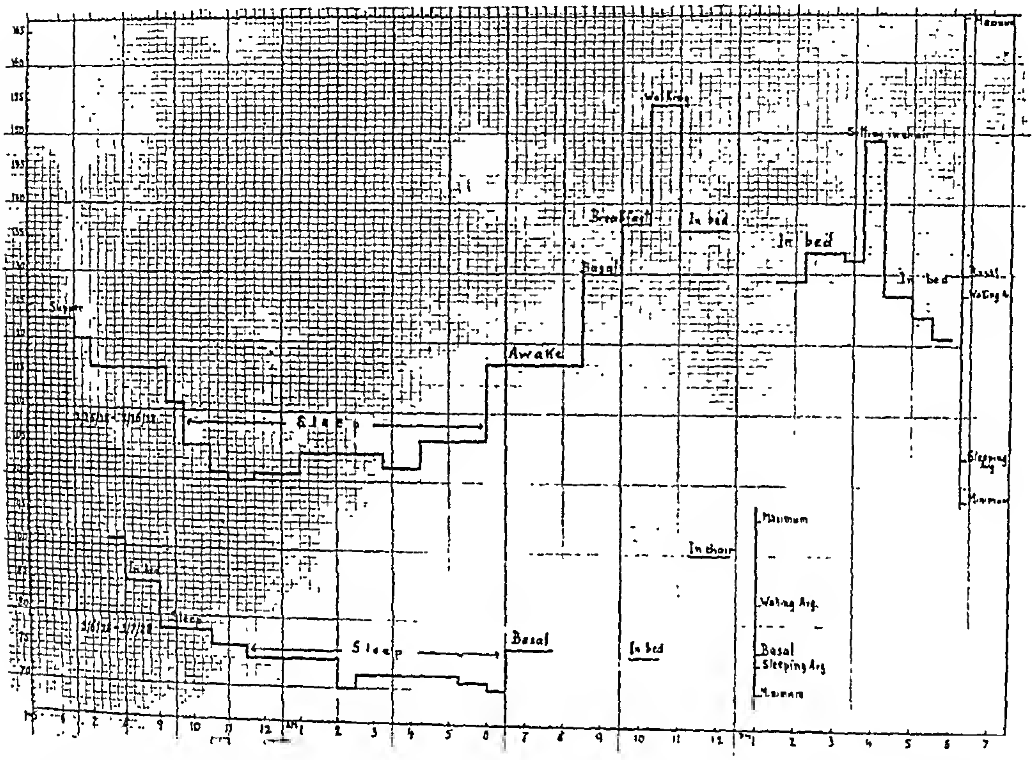

Fig. 8-a.—Auricular fibrillation; undigitalized. Total time 23 hours, 3 minutes. Total heartbeats 163,913.

b.—Auricular fibrillation; digitalized. Tincture of digitalis 24 c.c. from March 1-March 7. Total time 13 hours, 28 minutes. Total heartbeats 61,831.

seems to tolerate very large doses of digitalis without exhibiting any toxic action such as nausea or bigeminy.

Making due allowance for different rates of absorption and elimination in different individuals, this varying tolerance to the drug seems to be analogous to the well-known variation in tolerance of different persons to atropine. Patients with spastic colitis, for instance, tolerate infinitely larger doses of atropine than do other individuals. In the case of digitalis, those in whom there is apparent overactivity of the sympathetic nervous system are resistant to the action of the drug.

It would seem advisable in the labile group of patients with auricular fibrillation to supplement the action of digitalis with sedatives and

psychotherapy. It is also important to remember that these patients require larger quantities of digitalis than their body-weight calculation would indicate. The great value of rest and sleep as restoratives in cardiac insufficiency is evident from the graphs.

SUMMARY

The ventricular rate of patients with auricular fibrillation has been studied by means of the cardiotachometer. It has been shown that the ventricular rate is variable, that it accelerates in response to the slightest exertion or emotion, and that it slows during rest and particularly during sleep. All the evidence indicates that the ventricular rate in these patients is under control of the cardiac nerves and that alterations in rate are governed by neurogenically determined changes in conductivity of the specific conducting tissue of the heart. The changes in ventricular rate arise, apparently, in response to the varying physiological needs of the body just as in health, but the reaction is not so well regulated and is often excessive.

Patients with auricular fibrillation may be classed in two groups: those with labile and those with stable ventricular rates. The former are high-strung and nervous and correspond to patients with neurocirculatory asthenia. Their ventricular rates tend to be rapid, and quantities of digitalis in excess of the body-weight dose are required to keep the ventricular action slow and stable. In addition it would seem that sedative and psychotherapeutic treatment should assist materially in slowing the ventricles. In the stable group the ventricles do not exhibit such an exaggerated response to physical and emotional stimuli and can readily be kept under control by the usual methods of digitalis therapy.

The value of rest and sleep in the treatment of patients with auricular fibrillation, a fact well known, is forcefully demonstrated by actual count of the number of heartbeats by means of the cardiotachometer.

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THE ORAL ADMINISTRATION OF CALCIUM CHLORIDE IN CONGESTIVE HEART FAILURE*

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IN THE treatment of patients suffering from heart failure there are often present edema and collections of fluid in the serous cavities which are refractory to removal by drugs, such as digitalis, novasurol, and the theobromine diuretics which are commonly in use. For this reason it is desirable to test thoroughly measures which promise to be of benefit in these cases.

In 1921 and 1922 Blum[1] and his coworkers described a new group of diuretics. According to their conception edema is caused by the retention of sodium ions; sodium ions in being retained hold water which accumulates in the tissues and serous cavities. They found that diuresis was induced in cases of edema of nephritic origin, in cirrhosis of the liver with ascites and in inflammation of the liver with fluid accumulations by the oral administration of salts of calcium, potassium and strontium. They thought that the sodium ions in the tissues were replaced by calcium, potassium or strontium ions; that they were excreted as sodium chloride and in being excreted carried water with them. In this way water was removed from the tissues. They were of the opinion that diuresis occurred by the "replacement of ions." Though they believed that this group of diuretics was effective in the conditions just mentioned, they stated that they were usually ineffective in edema due to heart failure and gave warning that the use of them in these cases was dangerous.

At the time this series of papers appeared we had under observation a patient whom we were unable to free of edema by limitation of fluids, by the use of a diet free of salt or by the administration of digitalis and the usual diuretics. This patient we succeeded in making free of edema by giving calcium chloride by mouth. From this experience we were led to give the salt to a small number of patients; a preliminary report has already appeared.[2]

Since the appearance of Blum's papers, Keith, Barrier and Whelan[3] have reported the occurrence of satisfactory diuresis in cases in which there was edema due to nephritis, following the report of Atchley, Loeb and Benedict[4] concerning a patient who suffered from edema occurring in the course of diabetes. Recently, Segall and White,[5] after giving calcium chloride to a number of patients, concluded that it

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may be employed as a diuretic "in cases of cardiac failure with edema in which constant rest in bed, digitalization and administration of various diuretics have not resulted in satisfactory diuresis."

METHOD OF INVESTIGATION

Calcium chloride was administered orally to six patients suffering from heart failure in whom edema was present. All patients were subjected to a preliminary period of rest in bed. They were given a fixed amount of fluid per day. These conditions were maintained during the administration of calcium chloride. It was given as a concentrated solution. Divided into two doses, 15 gm. were usually given a day. It was followed by a small amount of orange juice for relief of the bitter taste. After taking calcium chloride patients complained occasionally of a burning sensation in the epigastrium or of abdominal cramps. These symptoms were, however, not severe. One patient (Case 3) vomited on one occasion and another (Case 2) on two occasions. Other untoward symptoms were not encountered. In some observations calcium chloride was given alone; in others it was given to patients who had first received a sufficient amount of digitalis to affect the T-wave of the electrocardiogram or to slow the ventricular rate in auricular fibrillation. In still further observations, the administration of calcium chloride was followed by that of digitalis. A few patients were the subjects of the three sets of observations. Most of the patients were those to whom other diuretics had been given without effect.

OBSERVATIONS

Case 1.—S. F. (See Case 18, Stewart[6]) was a woman, 24 years old. She was under treatment in the hospital from September 13, 1922, until July 29, 1924. The diagnosis* was: *Etiological:* acute rheumatic fever (inactive); *anatomical:* cardiac hypertrophy, mitral stenosis and insufficiency, aortic insufficiency, left ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. She was admitted to hospital because of shortness of breath and edema of the legs. She had suffered from numerous attacks of acute rheumatic fever between the ages of five and eighteen years. Cardiac involvement occurred at the time of the first attack. The heart was very much enlarged. There were signs of mitral stenosis and insufficiency and of aortic insufficiency. The systolic blood pressure measured 110 to 115 mm. of mercury and the diastolic 70 mm. Auricular fibrillation was present. From September, 1922, until June, 1923, the patient was given a diet free of salt, and the fluid-intake was restricted to 1500 c.c. a day. She was given digitalis either alone or combined with diuretin or theocin. By these means sporadic increases in volume of urine were obtained, but only rarely did the increase continue long enough to make the patient free of edema for even a day or two. Finally, the patient was given calcium chloride 15 gm. a day by mouth, on four days. Up to this time the volume of urine had been 1300 c.c. a day when she was taking 1500 c.c. of fluid a day. On the first day that calcium chloride was given the volume of urine was 1265 c.c., 673 c.c. on the second, 1575

*The diagnoses conform to the nomenclature for cardiac diagnosis approved by the American Heart Association. Am. Heart J. 2: 202, 1926-1927.

c.c. on the third, 1970 c.c. on the fourth, and 2210 c.c., 1706 c.c. and 1769 c.c. on the three days following, although *during* these calcium chloride was not given. The patient lost 0.8 kg. in weight, and the edema disappeared. Edema reappeared as soon as diuresis stopped, and on the third day after the end of diuresis, calcium chloride was accordingly given again on five days. One day only the output rose to 1800 c.c. Edema decreased. After an interval of three days (during which the volume of urine decreased to 400 c.c. per day, and edema increased) calcium chloride was given again. The day the administration of calcium chloride was begun, digitan 0.9 gm. was also given. The output rose to 1730 c.c., 1750 c.c., 1666 c.c., 1325 c.c., 800 c.c., and 1805 c.c. respectively on the six days that it was given and remained 1853 c.c., 1880 c.c., 1438 c.c., and 1790 c.c., on the four days afterward; it fell then to 1200 c.c. The patient lost 1.5 kg. in weight and became free of edema. She was given no drugs from June 27 to July 20. At the end of this time edema recurred and she gained 3.0 kg. in weight; the output of urine

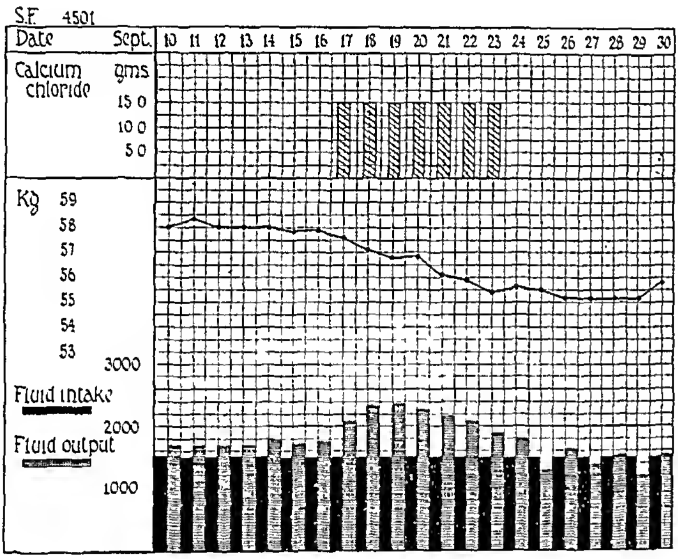

Fig. 1.—Shows the effect of the administration of calcium chloride upon the volume of urine in Case 1.

was approximately 1000 c.c. a day. Calcium chloride was then given on four days. On the first three days the output of urine was 705 c.c., 750 c.c., and 785 c.c., respectively. Diuresis did not begin until the fourth day when the output rose to 1595 c.c., and was 1695 c.c., and 2065 c.c. on the next two days. The patient lost 1 kg. in weight. Edema again decreased, and a few days later when digitan 0.7 gm. was given the output increased for a day or two and she became free of edema. She was given maintenance doses of digitalis. She was allowed to sit up; edema recurred, however, and she remained in bed. Beginning September 17 calcium chloride was given on seven days (Fig. 1). The output had been, on the average, 1700 c.c. a day before calcium chloride was given. During the seven days that calcium chloride was given, the volume of urine rose to 2060 c.c., 2362 c.c., 2178 c.c., 2284 c.c., 2190 c.c., 2085 c.c., and 1865 c.c. respectively; it was 1818 c.c. the next day and then fell to 1291 c.c. During the period of diuresis the patient lost 2.5 kg. in weight, and she became free of edema. She received no drugs from September 23 to November 12. Edema recurred. Calcium chloride was again given during five days. The output rose from 1000 c.c. to 1200 c.c. a day, to 1425 c.c., 1475 c.c., 2043 c.c., 1890 c.c., and 1890 c.c. respectively, and the patient lost 2 kg. At the end of this time there was only a slight trace of edema

of one ankle. The patient was then given digitalis; a slight increase in output of urine occurred. In spite of this, edema persisted and she gained weight. Beginning December 3, calcium chloride was given on five days. The output rose from 1400 c.c. to 1600 c.c., and remained at that amount for seven days.

Summary.—This patient with edema due to heart failure was given calcium chloride by mouth on seven occasions, four times alone and three times combined with full therapeutic doses of digitalis (0.7 gm. to 0.9 gm.). Diuresis followed on each occasion and on four of them she became free of edema. Calcium chloride appeared to be equally effective whether the patient was or was not under the influence of digitalis; the effect which could be ascribed to digitalis did not appear, however, to be greater when this drug was given in combination with

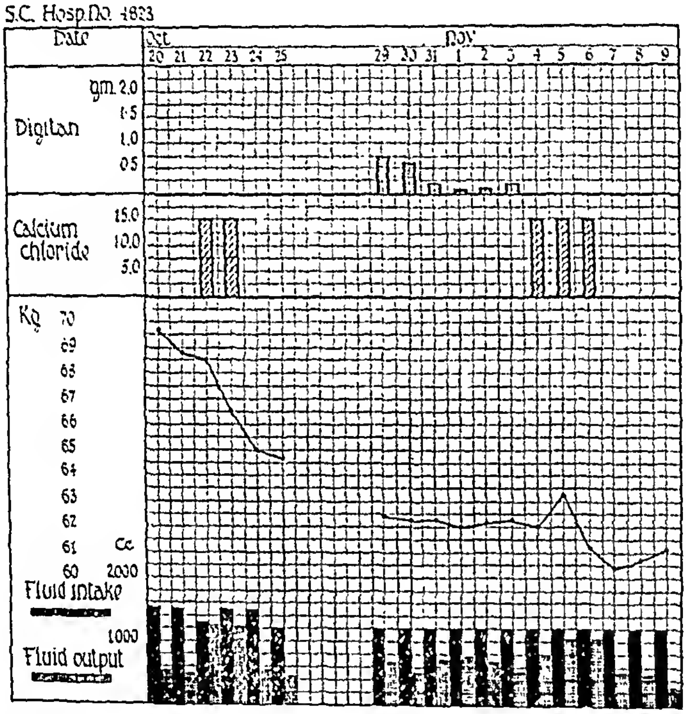

Fig. 2.—Shows the effect of the administration of calcium chloride upon the volume of urine in Case 2, first when given alone, and second when given after the administration of digitalis.

calcium chloride than when given alone, that is to say a synergistic action between these two drugs was not demonstrated in the case of this patient.

Case 2.—S. C. (See Case 14, Stewart[6]). This patient was a man, 66 years old. He was admitted to hospital complaining of shortness of breath of five years duration. The cardiac diagnosis of this patient was: *Etiological:* arteriosclerosis; *anatomical:* cardiac hypertrophy, mitral insufficiency, left ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. There was no history of acute rheumatic fever. The heart was enlarged. Auricular fibrillation was present. A soft systolic murmur was heard at the apex. The systolic blood pressure was 150 mm. of mercury and the diastolic 80 mm. Cheyne-Stokes respirations were present. There were moist râles at the bases of the lungs posteriorly.

There was marked edema of the legs. The Wassermann reaction of the blood was negative.

The fluid intake was limited to 1500 c.c. a day. After he had been in bed for three days he was given, on October 22, 1923, calcium chloride 15 gm. (Fig. 2). The output of urine, which had been 497 c.c. the day before rose now to 1210 c.c. The following day, when the same amount of calcium chloride was given it was 1226 c.c.; the edema disappeared. The next day calcium chloride was not given; the output of urine fell to 525 c.c. On October 25 the fluid intake was reduced to 1200 c.c. per day. The volume of urine remained low until October 26 and 27. On each of these days calcium chloride 15 gm. was given and the output rose to 621 c.c. and 1215 c.c. respectively; a decrease then occurred. The patient was given digitalis until the ventricular rate was slow and the electrocardiogram showed changes in the T-wave. There was one day (November 1) a slight increase in output to 770 c.c. He was then given calcium chloride 15 gm. a day on three days. The output amounted to 805 c.c. on the first, 1122 c.c. on the second and 1136 c.c. on the third day, but fell to 590 c.c. the next day when calcium chloride was not given. The patient was without medication for the next eleven days; the output of urine varied between 250 c.c. and 500 c.c. a day. A slight degree of edema recurred. Beginning November 18 he was given calcium chloride again, 15 gm. a day on 4 days. There was a slight but definite increase in output of urine amounting to 835 c.c. a day. During this time he lost weight and edema disappeared. He was then given digitalis from November 23 until December 10. Toward the end of this period the volume of urine was slightly increased, and he lost 2 kg. in weight. One day the volume of urine was 1100 c.c.; it then decreased. On December 12 he was given calcium chloride 15 gm.; the output rose from 770 c.c. to 1224 c.c. The next two days, when given the same amount of calcium chloride, it was 1105 c.c. and 1103 c.c. respectively; on the fourth day when he received calcium chloride 7.5 gm., the output fell to 516 c.c. and remained at that level. During the four days it was given he lost 2 kg. in weight. He was now given a sufficiently large amount of digitalis daily to keep the ventricular rate slow. About six weeks later acute dilatation of the heart occurred, and the patient died. An autopsy was performed. The diagnosis was as follows: General arteriosclerosis; arteriosclerotic involvement of the cusps of the aortic valves; cardiac hypertrophy; aneurysm of the abdominal aorta*; infarcts of the kidneys; arteriosclerosis of the kidneys; terminal broncho-pneumonia; venous stasis of the organs.

Summary.—Calcium chloride was given then on six occasions to this patient, on three without digitalis, on two, following the administration of digitalis, and on one the use of digitalis was followed by calcium chloride. The administration of calcium chloride was always accompanied by increase in volume of urine; it was often more than doubled on the days the drug was given. The resulting diuresis was sufficient to free the patient of edema. It appeared to be effective whether it was given when the patient was or was not under the influence of digitalis. Vomiting occurred twice during its administration.

CASE 3. I. K. This patient was a man 37 years old. He complained of shortness of breath, palpitation and edema. The cardiac diagnosis was: *Etiological:* unknown; *anatomical:* cardiac hypertrophy, mitral stenosis and insufficiency, right ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. Cyanosis was present. The heart was enlarged. There were signs of

*The patient frequently complained of abdominal pain. The abdomen presented no abnormality on physical examination.

mitral stenosis and insufficiency. The systolic blood pressure was 115 mm. of mercury and the diastolic 75 mm. There was free fluid in the right pleural cavity. Moist râles were heard in both lungs. The liver was enlarged; ascites was present. There was edema of the lower extremities.

The patient was so ill that digitalis was given at once. The ventricular rate became slow. While taking 1200 c.c. of fluid a day the output of urine remained between 295 c.c. and 519 c.c. per day. On the seventh day after admission to the hospital (the patient was still under the influence of digitalis) he was given calcium chloride 15 gm. The volume of urine on that day was 489 c.c. The following day, when calcium chloride was given again, the output was 618 c.c. On continuing its administration on the third and fourth days the output was 810 c.c. and 655 c.c., respectively. On the fifth day it was not given, and it fell to 524 c.c. Then it gradually decreased to 300 c.c. per day. Later, satisfactory diuresis occurred when novasurol was given.

Summary.—This patient was under the influence of digitalis when calcium chloride was given. There occurred a very slight increase in the output of urine. It was not sufficient, however, to have an effect on the accumulation of fluid in the tissues and serous cavities. Vomiting occurred once during administration of the salt.

CASE 4. G. B., (See Case 17, Stewart[6]). This patient was a man, 69 years old. He complained of shortness of breath and edema. The cardiac diagnosis was: *Etiological:* arteriosclerosis; *anatomical:* cardiac hypertrophy, aortic stenosis and insufficiency, mitral insufficiency, left ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. There was no history of acute rheumatic fever. The heart was enlarged; auricular fibrillation was present. Over the base there was a rough systolic and a soft diastolic murmur. Soft systolic and diastolic murmurs were also heard at the apex. The systolic blood pressure was 120 mm. of mercury and the diastolic 90 mm. There was free fluid in the right pleural cavity. The liver was enlarged; ascites was present. There was marked edema of the legs. The Wassermann reaction of the blood was negative.

The patient was given a large amount of digitalis. Diuresis did not occur. The output of urine remained 500 c.c. when he was taking 1000 c.c. of fluid a day. At a time when he was not under the influence of digitalis he was given calcium chloride 15 gm. a day on four days. On these days the output was 680 c.c., 755 c.c., 610 c.c., and 788 c.c., respectively. During this time there was no loss of weight, and the edema did not decrease. Later, after giving diuretin the volume of urine increased to 1588 c.c. on one day. About ten days later the patient died suddenly. An autopsy was performed. The diagnosis was: chronic cardiac valvular disease (aortic); general arteriosclerosis; perforation of the interventricular septum; contraction scar in the conus of the pulmonary artery; hypertrophy and dilatation of the right and the left ventricles; chronic myocarditis; thrombosis of the pulmonary artery; edema, ascites, hydropericardium; hydrothorax, venous congestion of the organs; arteriosclerosis of the kidneys; cysts of the kidneys.

Summary.—Calcium chloride was given to this patient when he was not under the influence of digitalis. The slight increase in output of urine which occurred was not sufficient to influence the degree of congestive heart failure.

CASE 5. A. B. This patient was a female, 44 years old. She complained of swelling of the abdomen, shortness of breath and edema. The diagnosis was: *Etiological:* acute rheumatic fever (inactive); *anatomical:* mitral stenosis and

insufficiency, cardiac hypertrophy, right ventricular preponderance; *physiological:* normal sinus rhythm, congestive heart failure. She suffered from an attack of acute rheumatic fever 7 years before. Involvement of the heart occurred at that time. Fluid had been removed from the abdominal cavity by paracentesis every three weeks during the last 20 months. The heart was enlarged. The rhythm was normal. There were signs of mitral stenosis and insufficiency. The systolic blood pressure was 100 mm. of mercury and the diastolic 80 mm. The lungs were clear. There was marked ascites. The liver was enlarged. There was marked edema.

During the first 5 days in hospital the patient gained 2.5 kg. in weight. The volume of urine was not more than 319 c.c. per day. Calcium chloride 10 gm. a day was given on 5 days. The output on these days was 315 c.c., 333 c.c., 474 c.c., 565 c.c., and 515 c.c., respectively. The next day, when it was not given, the output was 510 c.c. and then fell to 300 c.c. per day. Digitalis and novasurol were given also without diuretic effect. Ascites increased so rapidly that abdominal paracentesis was performed and 13 liters of fluid were removed. The patient died suddenly 4 days later. An autopsy was performed. The diagnosis at autopsy was as follows: chronic cardiac valvular disease (mitral stenosis); ascites; hydropericardium; chronic passive congestion of the liver, spleen and pancreas; chronic peritonitis, perihepatitis, perisplenitis; cirrhosis of the liver.

Summary.—The oral administration of calcium chloride to this patient was followed by an increase of only a few hundred cubic centimeters in the volume of urine. In this instance its use was not combined with the administration of digitalis.

CASE 6. E. A. This patient was a male, 72 years old. He complained of shortness of breath and swelling of the legs. The cardiac diagnosis was: *Etiological:* arteriosclerosis; *anatomical:* cardiac hypertrophy, chronic myocarditis, left ventricular preponderance; *physiological:* normal sinus rhythm, congestive heart failure. The heart was enlarged. The rhythm was regular. The sounds were clear both at the apex and over the base. The systolic blood pressure was 150 mm. of mercury and the diastolic 110 mm. There was fluid in the right pleural cavity. The liver was enlarged. Marked edema of the legs was present. The Wassermann reaction of the blood was negative with alcoholic antigen and positive with cholesterin antigen.

The patient was given 1200 c.c. of fluid a day. Calcium chloride, 15 gm. a day, was administered on 2 days. Increase in output of urine did not occur. It became necessary to remove fluid (1000 c.c.) from the right pleural cavity by paracentesis. Administration of digitalis, 1.3 gm. in 3 days, was followed by only a slight increase in output of urine. Fluid reaccumulated in the right pleural cavity, and 1200 c.c. of it were removed. Two weeks later calcium chloride was given again on 4 days; the administration of digitalis was continued, however. On the 4 days preceding the administration of calcium chloride the output of urine was 570 c.c., 782 c.c., 853 c.c., and 610 c.c., respectively. On the days it was given, the output rose to 886 c.c., 868 c.c., 1200 c.c., and 915 c.c. respectively. Diuretin and later theocin were given; no greater increase in output occurred than had resulted from the administration of calcium chloride. Calcium chloride was given again on 4 days. On this occasion increase in output did not occur. Although we were not able to induce diuresis by the usual measures, edema gradually diminished. Paroxysmal auricular fibrillation was often present. A hemorrhage, the origin of which was not discovered, occurred from the gastrointestinal tract. Later, strangulation of an inguinal hernia occurred, and the patient was removed to another hospital for operation. The patient died a few days later. An autopsy was not performed.

Summary.—In this patient there was severe cardiac decompensation. On two occasions the use of calcium chloride was without effect on the volume of urine. On another occasion, when combined with the use of digitalis, a slight increase occurred.

SUMMARY

Calcium chloride was given orally to six patients suffering from edema due to heart failure (Table I). Slight increase in the output of urine occurred, but marked diuresis was not observed. The administration of digitalis simultaneously with the oral administration of calcium chloride did not appear to be more effective than its use alone. The observations were repeated on several occasions on each patient. In two patients only was diuresis sufficient to free them of edema.

TABLE I

SUMMARY OF RESULTS FOLLOWING THE ADMINISTRATION OF CALCIUM CHLORIDE

CASE NO.	CALCIUM CHLORIDE				NUMBER OF OBSERVATIONS ON EACH PATIENT
	WITHOUT DIGITALIS		WITH DIGITALIS		
	DIURESIS	NO DIURESIS	DIURESIS	NO DIURESIS	
1	4*		3*		7
2	3*		3*		6
3				1	1
4				1	1
5		1			1
6	2*		1		3
TOTAL	9	1	7	2	19

*Refers to number of separate observations.

DISCUSSION

We have observed an increase in the output of urine following the oral administration of calcium chloride. Diuresis was never very marked, and in only two patients was it effective in decreasing edema. The results in even these two patients are contrary, however, to Blum's statement that the salt was without diuretic effect in edema due to heart failure. Nor did we observe deleterious effects following its administration. It may be recalled that Blum was of the opinion that cardiac patients do not tolerate the drug.

The mechanism by which calcium chloride acts as a diuretic is not known. Hjort[7] and Salvesen, Hastings and McIntosh[8] and others[4, 9] have found that the administration of it by mouth produces a severe uncompensated acidosis in dogs and in human subjects. This is due to a replacement of the HCO_3 radicle by Cl in the blood, as the result of absorption from the alimentary tract of the Cl of calcium chloride without Ca. There is an actual loss of base from the blood and a failure to adjust the carbon dioxide tension to the lowered bicarbonate. The calcium content of the blood serum may increase or may be unchanged. On the other hand the intravenous administration of calcium

chloride has no effect on the acid-base equilibrium of the blood; there occurs, however, a moderate rise in the phosphates. The injected calcium leaves the blood in from three to six hours. Whether the diuretic effect is dependent on the presence of the anion or upon the acidosis or upon some other mechanism is at present unsettled.

CONCLUSIONS

1. The administration of calcium chloride to cardiac patients with edema increases the volume of urine.

2. The increase in output which results is only occasionally effective in decreasing edema.

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OBSERVATIONS ON THE MECHANISM OF RELATIVELY SHORT INTERVALS IN VENTRICULOAURICULAR AND AURICULOVENTRICULAR SEQUENTIAL BEATS DURING HIGH GRADE HEART-BLOCK*

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A NUMBER of cases have been reported with electrocardiograms which displayed, in the presence of otherwise complete heart-block, ventriculoauricular sequences with brief intervals between ventricular and auricular contractions. The auricular elements of these sequences have been represented by abnormally shaped and usually inverted waves. Some observers have attributed these abnormal auricular beats to rapid retrograde transmission of the impulse. Thus Danielopolu and Danulesco[1] suggest that retrograde conduction may be preserved after forward conduction is lost, and they raise the question as to whether the pathways of forward and retrograde transmission may not be different. Veil and Codina-Altes[2] have recently also supported the hypothesis of retrograde conduction. On the other hand, Cohn and Fraser[3] proposed the hypothesis that the abnormal auricular beats are due to the mechanical stimulus of the contracting ventricular mass acting on auricular tissues. Wilson and Robinson[4] in discussing a case reported by them state that it must be assumed that ventricular systole hastened the discharge of a stimulus in the lower auricular or upper junctional tissues. Barker[5] who has recently written on this subject adopts a view which is essentially one of mechanical stimulation. He assumes that the contracting ventricle stimulates mechanically the His bundle above the lesion producing block and that the impulse is then transmitted in a retrograde manner through the A-V node to the auricles. These references are perhaps sufficient to indicate that the nature of the mechanism of retrograde sequential beats occurring during high grade heart-block is uncertain; no convincing evidence has thus far been produced.

The change back and forth in rhythm from otherwise complete heart-block to auriculoventricular sequential beating with normal transmission intervals has also been observed several times. In these cases the view seems to have been accepted by all writers on the subject that the sequential beats were due to transmission of the excitatory process through the junctional tissues. Carter and Dieuaide[6] believe that the

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bundle may contain only a few intact fibers which are just equal to the work of transmission under favorable circumstances but fail when stress occurs. The few cases of this nature in which anatomical study of the junctional tissues was subsequently made have all shown comparatively few fibers present capable of transmitting the impulse. The nature of the stress determining their failure to function at times is not known; possibly it is concerned with variations in blood supply to the bundle. We shall discuss this point later.

Our interest in these phenomena was aroused in 1922 by the finding, in a patient with otherwise complete dissociation, of isolated auriculoventricular and ventriculoauricular sequences having P-R and R-P intervals of approximately 0.16-0.17 second in the same strip of tracing. Frequent studies of this patient were made during the remaining five years of her life, and remarkable shifts back and forth among complete block, incomplete block and apparently normal rate of transmission were observed. Following her death, permission was granted to remove the heart; and serial sections of the bundle and of the upper part of the main branches were made. These studies are reported under Case 3 of our group.

We have encountered ventriculoauricular sequences with comparatively brief R-P intervals and abnormally shaped P-waves in the electrocardiograms of several cases of high grade heart-block and regard this finding to be much commoner than the literature suggests. In two of the cases the behavior was somewhat different from that of any previously reported and should be taken into account in the formulation of hypotheses to account for the mechanism of retrograde beats during high grade block.

Case 1.—J. W., a man 60 years old, was admitted to the Medical Division of the Philadelphia General Hospital, Dec. 4, 1924, in a state of severe heart failure. There was present marked arteriosclerosis. The heart was greatly enlarged and showed evidences of aortic insufficiency. The rate was about 30 beats per minute and there were brief attacks of unconsciousness (Stokes-Adams syndrome).

An electrocardiogram made two days after admission (Fig. 1) showed a regular ventricular action of 28 beats per minute and an auricular rate of 50 beats per minute. The auricular rhythm was slightly irregular due to the fact that occasionally slightly premature ectopic auricular beats were in some way initiated by the preceding ventricular beat. In these sequences the R-P intervals measured approximately 0.16 second. The ectopic auricular beats were never highly premature occurring only late in the expected interauricular interval. In each instance the returning auricular cycle was slightly longer than those of the dominant auricular rhythm.

A tracing made six days later is shown in Fig. 2. At this time there was practically continuous coupling of ventricular beats. The first beat of each couple was of the usual idioventricular type, and the second was an extrasystole probably also arising in the junctional tissues. Both types of ventricular beats initiated premature ectopic auricular beats.

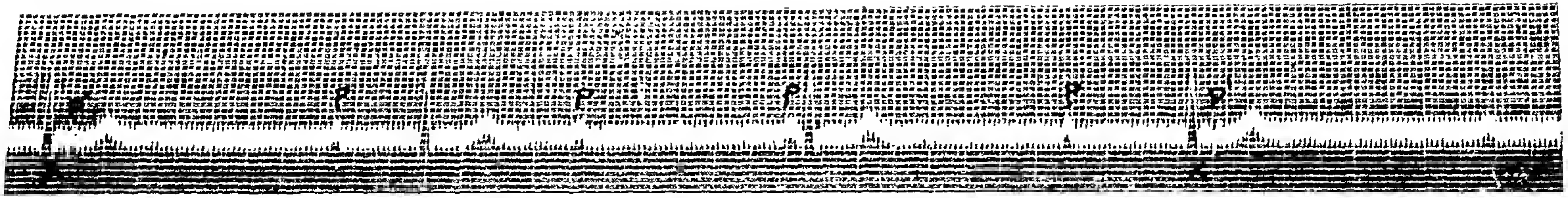

Fig. 1.—Case 1. Regular idioventricular rhythm, rate 28, with two ventriculoauricular sequences (*X*).

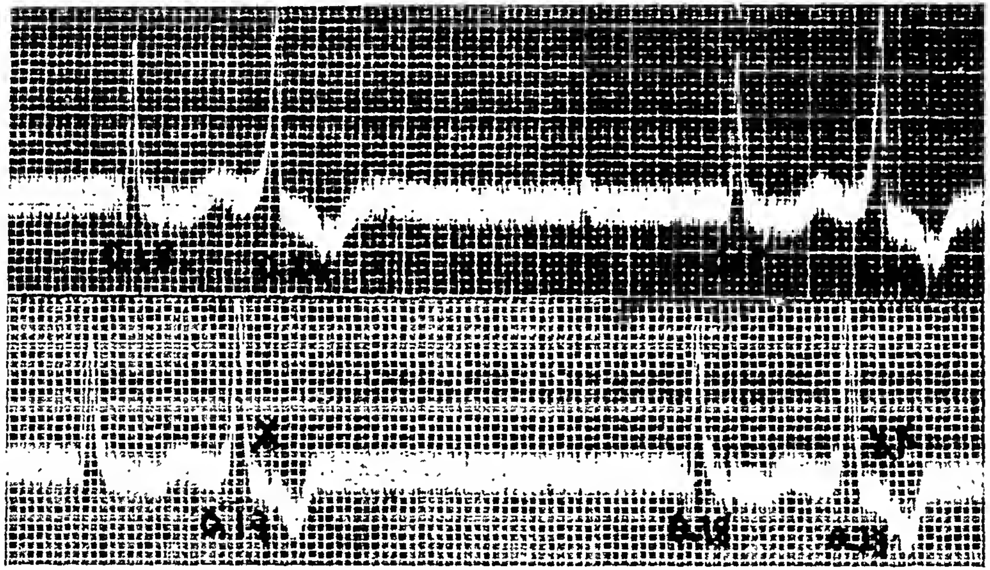

Fig. 2.—Case 1. Idioventricular rhythm with paired ventricular beats; each ventricular beat of the top strip forces auricular response. The R-P interval of the first sequence of each pair is 0.18 second, and the second sequence is 0.24 second. In strip 2, in the sequence marked *X*, the R-P interval is 0.19 second. The interval is shorter when the first ventricular beat of a pair does not force auricular response.

In strip 1, Fig. 2 (Lead II), the first sequential beat of the couples shows an R-P interval of approximately 0.18 second*, while the second sequence shows an R-P interval of 0.24 second. In strip 2, Fig. 2 (Lead III), there is no aberrant auricular beat following the first ventricular beat of the first couple. The sequence in connection with the second beat of the couple has an R-P interval of 0.19 second. In the following couple, both of which show ventriculoauricular sequences, the first R-P interval is 0.19 second and the second R-P interval 0.23 second.

COMMENT

Case 1 seems to furnish evidence bearing on the question as to whether the abnormal auricular beats of retrograde sequences are excited by mechanical stimulation or a transmitted (conducted), excitatory process. The fact that when two ventriculoauricular sequences occur in succession in connection with coupled ventricular beats, the second R-P interval is longer than the first suggests that the mechanism is one of conduction rather than mechanical stimulation. To this view, however, the objection might be raised that the differences in R-P intervals might be accounted for by the fact that the second ventricular beat was different mechanically from the first as shown by the altered electrocardiographic curve and the less time available for ventricular filling so that the mechanical stimulus to the auricle might be delayed. This objection is met by consideration of the effects of presence or absence of an R-P sequence in the first of coupled beats on the length of the R-P interval in the second beat of a couple as is shown in Fig. 2, strip 2.

It seems clear from these data that when two retrograde sequences occur as close together as 0.68 second there is a prolongation of the second sequence. This delay cannot be attributed to the fact that the second beat of the couple is premature, weak, or aberrant, since it does not occur when the first ventricular beat of the couple fails to force an auricular contraction.

We regard the above as strong evidence for the view that the abnormal auricular beats are stimulated by retrograde conduction of the excitatory process.† There is further evidence of a somewhat different nature. If one observes the time in the auricular cycle when the auricular element of the retrograde sequences occurs, it is found not only in our Case 1 but also in all cases we have studied and all tracings we have seen in published reports that they occur only late in

*These intervals were measured repeatedly with a Lucas comparator until a fair degree of consistency was obtained in the third decimal place. We therefore believe the figures to be accurate ± 0.005 second. The variations in transmission intervals pointed out are so wide, however, that high grade accuracy in measurement would not be necessary to determine them.

†It would seem out of the question to explain differences in R-P intervals of this magnitude by variations in latent intervals of auricular muscle. Available evidence seems to indicate that the latent interval of mammalian heart muscle is extremely brief.[7]

the expected interauricular interval.* It is precisely at such a time that the junctional tissues should be recovering their maximum functional capacity because of the lapse of time following the effort to transmit downward the preceding normal type of auricular beat. In connection with our Case 2 we shall attempt to show how a preceding period of unusually long rest in the bundle is followed by a relatively short ventriculoauricular sequence.

While the inexcitable period of junctional tissues, particularly if damaged, may be relatively long, that of auricular muscle is relatively short. There would thus seem to be no good reason, if the auricles were being excited by mechanical stimulation, why the responses should be limited to the latter part of the expected interauricular interval.†

One hesitates, in the present state of our knowledge, to accept an hypothesis assuming the occurrence of prompt retrograde conduction when forward conduction is either markedly delayed or fails com-

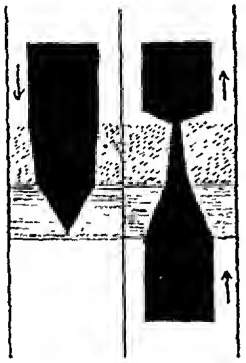

Fig. 3.—A diagram illustrating the conception of unidirectional transmission through junctional tissues. The solid black represents the excitatory process. As it descends (left) its vigor is impaired by a slight barrier to conduction (dotted area) just enough that it is unable to traverse a greater barrier (ruled area). The ascending (retrograde) excitatory process (right) meets the greater barrier before being subjected to decrement and is therefore able to pass it and avoid being blocked.

pletely, yet the data we have presented in Case 1 and shall present in Cases 2 and 3 demand its consideration. We find no precedent in the literature for such behavior, although so-called undirectional block from ventricles to auricles has been observed in several cases.[8] One can therefore only speculate as to the possible nature of a lesion permitting only unidirectional retrograde transmission. Conceivably it might be determined by the location of the chief barrier to conduction with reference to other secondary barriers. If we assume that the

*The incidence has been commented on by others. There is one apparent exception found in a tracing published by Danielopolu and Danulesco[1] during vagal stimulation in which an inverted P-wave of the type under discussion occurred shortly after a normal P-wave. In this case, however, there was said to be no conduction defect. Under such circumstances escape from vagal inhibition might readily have permitted transmission to occur.

†The chief objection to the compromise hypothesis of Barker[5], to the effect that the ventricles mechanically stimulate the junctional tissues above the area of block whence the impulse is carried to the auricles in a retrograde direction through the A-V node, is the short R-P intervals. There would not seem to be time for the occurrence of this double mechanism.

descending excitatory process is subjected to decrement in its downward path, it might be unable to traverse the final most serious obstacle whereas an excitation from below might be able to traverse the serious obstacle and be transmitted through the less important barriers to conduction. The point may perhaps be made clearer by the analogy to a runner who might be able to jump a broad stream at the beginning of his race and then overcome relatively minor obstacles, whereas if the minor obstacles had come first he might have been so fatigued as to be unable to jump the broad stream.

In Fig. 3 we have attempted to diagram this conception of unidirectional transmission.

Case 2.—Mrs. F., 37 years of age, was referred for examination, June 23, 1923, to the Heart Station of the University Hospital. She had consulted her physician because of attacks of vertigo. He, noting that the pulse was slow and somewhat irregular, requested an electrocardiogram.

The tracing (Fig. 4) shows two-to-one heart-block. There are present two types of auricular arrhythmia. One of them is a form of sinus arrhythmia, the auricular cycles which contain QRS complexes tending to be shorter. The other form of auricular arrhythmia is due to fairly frequent premature ectopic beats following ventricular beats. These ectopic beats, as in Case 1 are found only toward the latter end of the expected auricular cycle. The R-P intervals are all approximately 0.26 second in duration except the R-P interval found after a premature beat (X) which is 0.22 second.

COMMENT

In Case 2 two modes of stimulation suggest themselves as possible mechanisms by which the ectopic auricular beats are excited: (1) reciprocating beats, and (2) mechanical stimulation.

Mines[9] in 1913 described an abnormal mechanism which he was able to produce by rhythmic stimulation of the heart of the electric ray and the frog, which he called reciprocating rhythm. The rhythm of each chamber (auricle or ventricle) seemed to be dependent on the other, and the alternate contractions spaced approximately evenly would continue for long periods unless interrupted by a stimulus. The mechanism could be initiated by an extrasystole or when already present stopped by an extrasystole. Mines regarded the condition as a circulating mechanism. He offered the suggestion that under rapid stimulation different fibers would recover at different rates and the impulse going in one direction through certain fibers would go in the opposite direction through other fibers.

White[10] and Drury[11] have reported clinical cases which appear to be examples of reciprocating beats and Drury has called attention to the similarity of the mechanism in his case with that produced experimentally by Mines. In their cases, however, the impulse apparently arose in the junctional tissues and spread to both ventricles and auricles. When conduction was strained so that the auricular beat was delayed, an impulse would descend to the ventricles and a second

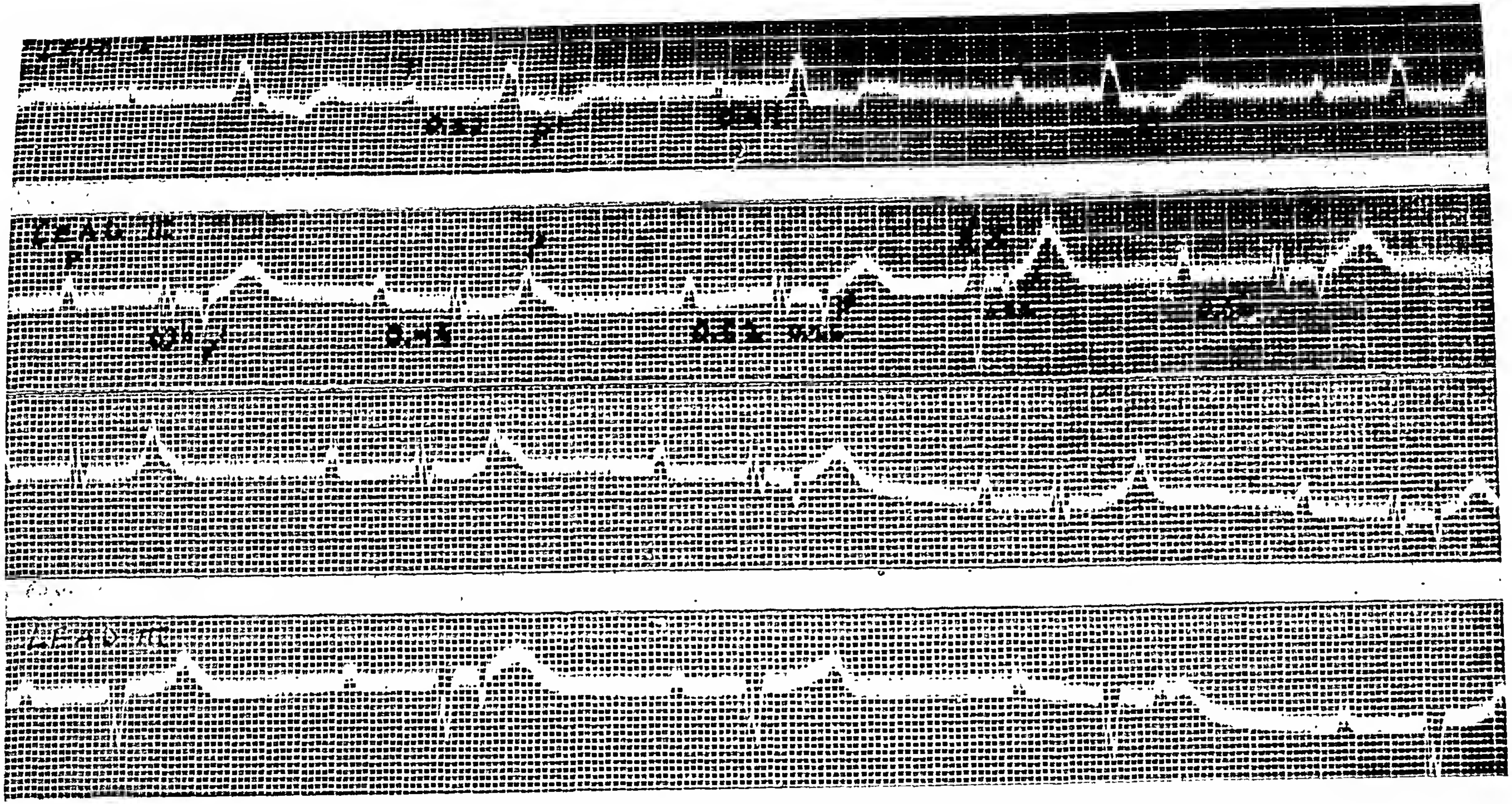

Fig. 4.—Case 2. Two-to-one heart-block. Reciprocal beats each with a sequence consisting of normal type auricular beat, long P-R interval (0.52-0.56 second), ventricular beat, R-P interval of 0.26 second and ectopic auricular beat.

The R^1-P^1 interval in connection with the premature ventricular beat in Lead II (X) is 0.22 second. This aberrant auricular wave is not so deeply inverted as the others. It falls just at the time a normal auricular wave is expected and probably inscribes the combination of a normal beat spreading from the sino-auricular region plus the ectopic beat.

ventricular beat occur. Gallavardin and Gravier[12] demonstrated in a case of A-V nodal bradycardia that by vagal stimulation and thus lengthening R-P intervals, reciprocating beats could be produced. Scherf and Shookloff[13] have recently made an experimental study of reciprocating beats (umkehr Extrasystolen) and believe the site of reversal to be in the upper part of the nodal tissue. So far as we are aware no clinical case has been described previously in which the course of the reciprocating beats was from auricle to ventricle back to auricle again. In our case it is obvious that conduction was in a critical condition, the state insisted on by most workers as necessary for the production of reciprocating rhythm. The one objection, so far as we are aware, which may be raised against this interpretation is the fact that retrograde transmission must be assumed to proceed more rapidly than forward transmission. It has been shown repeatedly in experiments that conduction is more readily accomplished from auricles to ventricles than from ventricles to auricles and that A-V intervals

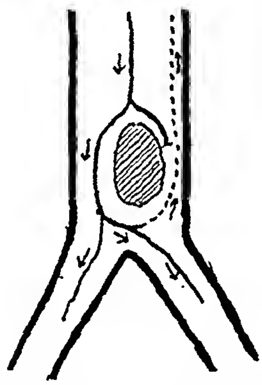

Fig. 5.—A diagram illustrating the conception of reciprocal beats in Case 2. The oval ruled area represents a lesion in the bundle of such a character as to cause the formation of two pathways, both offering obstacles to conduction but the one on the right more than on the left. Each alternate descending impulse is transmitted down the left side but is blocked on the right. The left descending impulse after passing the lesion spreads not only to the ventricles but also upward on the right side of the lesion. Some of these impulses are transmitted back to the auricles. The successful retrograde transmission is due either to (1) longer recovery period due to block of descending impulse on right side or (2) position of barriers to conduction permitting only unidirectional (in this case, retrograde) transmission. See Fig. 3.

tend to be shorter than V-A intervals. However, the evidence presented in our Case 1 which seems to indicate that in at least one case retrograde transmission has been successfully accomplished even though forward conduction from auricles to ventricles was lost, justifies consideration of the possibility that in lesser grades of block, A-V intervals might exceed V-A intervals. Any alternative hypothesis would seem to involve the assumption of mechanical stimulation of auricles by contracting ventricles. To this view there are the following objections:

1. The incidence of the ectopic auricular beats is always late in the auricular cycle. The significance of this fact in its relationship to the relative probability of transmission or mechanical stimulation has already been discussed in the presentation of Case 1.

2. The R-P intervals are much longer than in any of the cases in which mechanical stimulation was proposed as the mechanism. One must therefore assume that the mechanical stimulation has in some way been delayed. In view of the unusually long forward transmission intervals, however, one might reasonably expect delayed retrograde transmission also.

3. We are unable to account for the shorter R-P interval after an extrasystole (X in Fig. 4) on the basis of mechanical stimulation. It is readily accounted for on the basis of retrograde transmission since the rest period preceding this beat is decidedly longer than any others preceding ectopic auricular beats. The longer rest period may therefore account for accelerated transmission of the next beat.

For these reasons the hypothesis of mechanical stimulation seems inapplicable to this case; and we, therefore, favor the interpretation of a circulating mechanism similar to that proposed by Mines. It is probable, however, that in the clinical cases the mechanism is not identical with that observed by Mines, since continuous transmission back and forth between auricles and ventricles has not been observed. Possibly in such a case as ours the mechanism is due to peculiarity in the location of a lesion in the bundle resulting in two pathways with slightly unequal conductive capacity joined above and below the lesion in such a way that a circulation of the excitation could occur (Fig. 5).

CASE 3.—Mrs. A. H. S., a white woman, 48 years old, was admitted to the Medical Division of the University Hospital Sept. 8, 1923, complaining of "thumping of the heart." The history dated back to 1912 when she had an attack of syncope with nausea and vomiting. At that time she was informed that she had a weak heart. In 1914 she was told that her heart rate was unusually slow. During the following years the slow rate (usually about 30 beats per minute but sometimes as low as 13 beats) had occasionally recurred. Since January, 1923, her difficulties had increased markedly. She was bothered by almost constant thumping of the heart, pain and sense of constriction in the chest, frequent attacks of vertigo and occasional syncope. In the spring she entered the Lankenau Hospital and was told that she had heart-block, although no electrocardiograms were made. During the summer she was admitted to the Philadelphia General Hospital. At this time electrocardiograms showed the presence at times of complete heart-block, and at other times various manifestations of incomplete block.

The past medical history is unimportant except for the suspicion of tuberculosis in 1914, but studies carried out in a sanatorium were negative. Her habits have always been good. She has always done housework with occasional short periods of work in a mill. Her father is said to have died of heart disease, her mother of apoplexy, and of 7 siblings, one brother has heart disease and two sisters have had tuberculosis. Two of her three children are said to have heart disease.

Physical Examination.—The patient was a sallow, poorly nourished woman who looked older than her stated age. She was obviously weak but able to walk about the ward. Nearly all teeth were missing. The tonsils were small and innocent in appearance. The thyroid was slightly enlarged. The lungs showed evidences of an old lesion at the right apex. The heart was not enlarged. The rate was 30 beats per minute and the rhythm regular. There was a systolic apical murmur.

and in the third interspace to the left of the sternum a distinct short sound was heard about midway between beats. The peripheral arteries appeared to be in good condition, and the retinal vessels showed no abnormality. The blood pressure was 135/70 mm. The liver was enlarged, extending 8 cm. below the costal margin in the midclavicular line. The spleen was barely palpable.

Several blood counts were normal. All blood Wassermann tests were negative. The urine showed traces of albumin and hyaline casts from time to time but was otherwise negative.

On the first admission to the University Hospital the patient remained in the ward from Sept. 8, 1923, to Dec. 23, 1923. During this time she showed wide variations in cardiac behavior. There was a period of several days during which complete dissociation was present. No drugs had been taken prior to this period of block. On one occasion there was an attack of syncope which developed while she was being examined. The radial pulse disappeared entirely, and no heart sounds were heard. An intracardiac injection of epinephrin was ordered, but

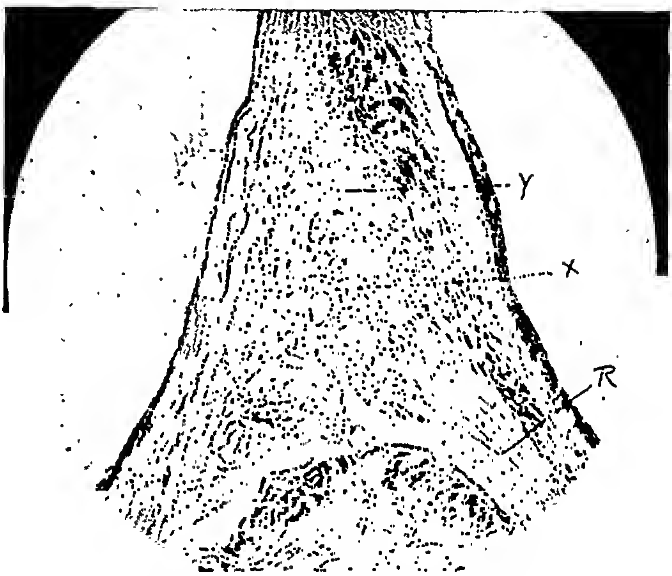

Fig. 6.—Shows the main bundle of His (*X*) and the right branch (*R*). In the upper portion of the main bundle is shown a defect (*y*).

just as it was to be given heart sounds and pulse reappeared. A second, apparently similar attack occurred during the night.

Usually the mechanism was 2-to-1 block, at other times 3-to-1, 3-to-2, and for long periods no block would be apparent. Rates as high as 140 beats per minute were observed with all beats transmitted. Prolongation of transmission intervals was never observed.

There were four subsequent admissions to the University Hospital. While she was at home, she was under the care of one of us. Consequently she was under fairly close observation for over five years. It was observed that marked bradycardia always caused a great deal of distress, and this was the reason for each admission to the hospital. On the first three admissions the block disappeared after varying periods of complete rest. On the fourth admission barium chloride seemed to help abolish the block. The final admission was on Dec. 13, 1927. This time the idioventricular rhythm persisted in spite of treatment (complete rest and barium chloride); the rate grew progressively slower, and the circulation seemed to fail more or less proportionately. Death occurred Jan. 10, 1928.

Permission for necropsy was limited to the heart. Nothing noteworthy was discovered on gross examination except a small area of fibrosis in the septum centering about the region of the branching of the bundle. The heart was not enlarged; there were no pericardial adhesions and no valvular defects. The larger coronary vessels showed some evidences of arteriosclerosis, though at no point, so far as gross dissection revealed, was the lumen encroached upon.

Histological Studies of Junctional Structures

The block of tissue sectioned serially included the conducting tissue from the lower portion of the A-V node to well beyond the point of division of the main bundle into its two branches.

The A-V node and the upper half of the main bundle were relatively normal histologically. Approximately half-way down the main bundle a small area of round-cell infiltration appeared. From this point on, the main bundle became increasingly pathological, there being more and more interstitial fibrosis and several minute areas of beginning calcification. The small ramifications of the coronary

Fig. 7.—Shows the same area further forward. The whole of the main bundle is replaced by the defect, only one small area of muscle (X) being seen.

arteries showed thickening, this going to the point of practical occlusion in some instances. In spite of the pathological condition of this region of the bundle the individual muscle fibers appeared relatively good.

When the region of the division of the main bundle into its branches was approached, not only were changes of the same order still in evidence but also there appeared a degenerative lesion that resulted in destruction of the involved portions. This lesion was conical in shape with its apex pointing posteriorly. Studying this portion of the bundle from behind forward, approximately the first eighth of its diameter presented the same appearance as the higher levels; namely, fairly healthy individual muscle fibers in the midst of greatly increased interstitial fibrous tissue. Further in front of this posterior eighth of the bundle the apex of the destructive lesion appeared. This enlarged in all directions conically as the front of the bundle was approached. As the lesion became extensive, it dipped well down into the anterior portion of the right branch. The left was not involved. The lesion itself showed a complete absence of muscle fibers, and in their stead was seen a reticulum of large rounded spaces that apparently were the re-

mains of fat cells, the fat itself having been dissolved out in the process of fixation.

The condition of the right branch remains to be described. The large lesion of the main bundle dipped down into this branch in its anterior portion and destroyed it for a definite distance. In the posterior portion of the right branch, another lesion, apparently independent but probably of the same nature, was present. The section here happened to show the fibers cut absolutely longitudinally. The muscle fibers were entirely gone with only a fibrous reticulum remaining, giv-

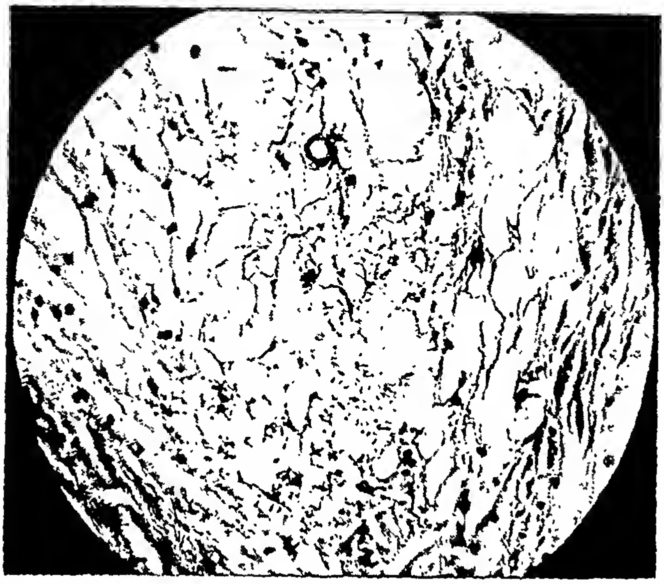

Fig. 8.—Is a high-power photomicrograph taken from the same area. The muscle fibers in this area are completely gone except for a small group of fibers in the lower left corner of the illustration. In place of the muscle fibers are large empty spaces enclosed by a reticulum of fibrous tissue that are presumed to have contained fat.

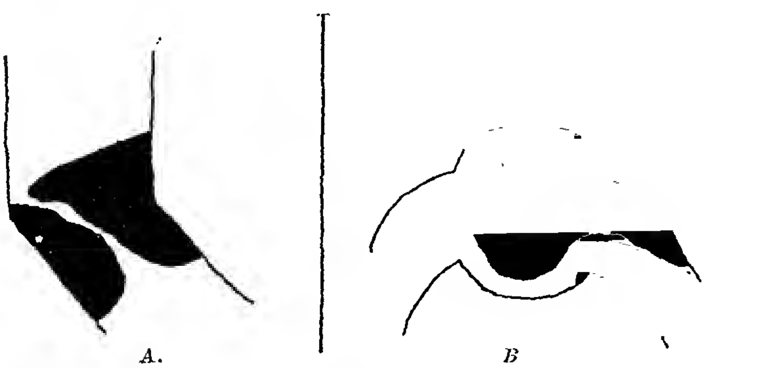

Fig. 9.—A schematic drawing of the destructive lesions (shaded) in the main bundle and its right branch. *A*, lateral view of main bundle and right branch; *B*, looking down on main bundle and branches.

ing the appearance of the strings of a harp. The nature of the degenerative lesion that resulted in this appearance seemed doubtful to us. Perhaps a fatty change, similar to that causing the big lesion of the main branch is the most likely explanation (Figs. 6, 7 and 8 show the destructive lesion in the main bundle).

The two lesions in this branch, one anteriorly and one posteriorly, almost came together. However, between the two there were relatively few strands of conducting muscle. These fibers were distinctly atrophic, stained poorly and were clearly far from normal. However, we believe that under certain conditions these fibers did successfully transmit impulses.

Summary of Findings.—There was a lesion of the main bundle that completely destroyed those portions involved. This lesion failed to involve an area of the bundle on the left side and posteriorly equaling approximately one-eighth of the total diameter of the bundle. Furthermore, the lesion being conical in shape, resulted in there being slightly more undestroyed tissue around its narrowed apex than around the wider base. However, the narrow band of undestroyed bundle was the seat of round-cell infiltration, areas of early calcification, arterial disease and increased fibrosis. These changes resulted in individual groups of muscle fibers being so separated from other groups that it seems quite probable to us that conduction was interrupted.

The right branch showed complete destruction except in its central portion where a relatively few fibers that were definitely diseased probably afforded a path of conduction under certain circumstances at least. (Fig. 9 is a schematic representation of the destructive lesion in the main bundle and its right branch.)

Description of Electrocardiograms

We have selected from the numerous tracings made, only those which seem to be representative of peculiar variations in mechanism observed.

The tracing in Fig. 10 shows complete dissociation, occasionally interrupted by slightly premature ventricular beats (X) each bearing an exact relationship to the preceding auricular beat and obviously excited by the auricular beat. These premature ventricular beats are all aberrant in form. There is also found some auricular arrhythmia due to slightly premature aberrant auricular beats (XX) each bearing a relationship to the preceding ventricular beat and obviously excited by it. The P-R intervals are 0.15 second and the R-P intervals 0.16 second. The premature auricular beats are similar in type to those recorded in Cases 1 and 2, but the R-P intervals are shorter than those found in Case 2.

That the aberrance of the ventricular beats excited by auricular contractions is not due to their prematurity is shown in Fig. 11 in which two highly premature beats (X) are found to have normal type complexes. These two beats are probably junctional extrasystoles arising below the level of the block. This view is favored by the fact that they are accurately coupled with preceding ventricular beats and not with auricular beats.

In Fig. 12 there are shown various manifestations of sequential beating. In strip 1 is seen the end of a paroxysm of auricular tachycardia in which all auricular beats stimulated ventricular response. In strip 2, there is 3-to-2 block, in strip 3, 2-to-1 block and in strip 4, 3-to-1 block.

In Fig. 13 we see the shift from 2-to-1 rhythm to complete dissociation. The first three ventricular beats recorded are aberrant as always occurred with sequential beating. The P-R intervals were approximately 0.16 second. At the fourth ventricular beat ventricular escape begins to assert itself, and by the sixth beat it is complete. The fourth and fifth beats are transition forms.

Effect of Vagus Stimulation.—Vagus stimulation was tried many times during periods of incomplete block. The methods employed were pressure on either right or left vagus in the neck, pressure on both sides simultaneously and ocular pressure. The auricular rate could be slowed by vagus stimulation, but on no occasion did higher grade block result.

Effect of Drugs.—Repeated intramuscular injections of atropin were made with electrocardiograms taken just before injection and every fifteen minutes up to from two to three hours after injection. The dosage employed was usually 3 mg. of atropin sulphate, but twice during periods of 2-to-1 rhythm 6 mg. were used.

Atropin in these dosages invariably caused acceleration of the auricular rate. Associated with this acceleration, an original 1-to-1 sequential rhythm might be

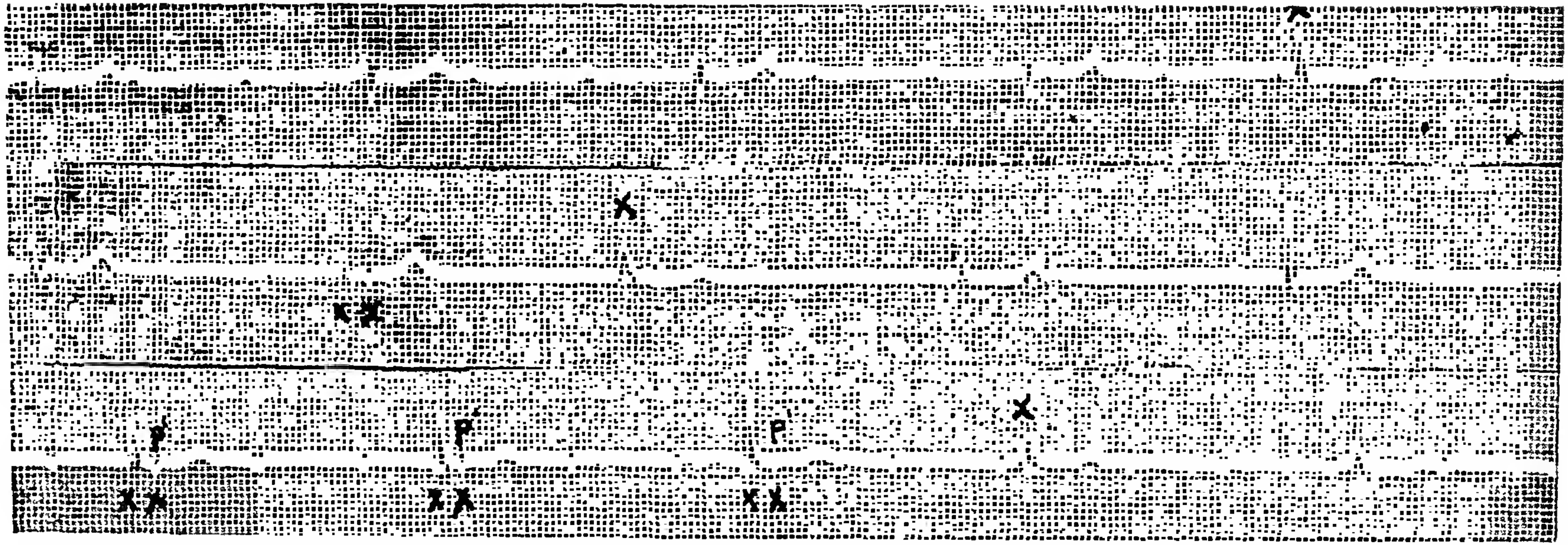

Fig. 10.—Case 3. High grade heart-block with isolated brief auriculoventricular sequences (marked with x above) and brief ventriculo-auricular sequences (marked with xx below). In the A-V sequences the ventricular complexes are invariably aberrant, and in the V-A sequences the auricular complexes are aberrant.

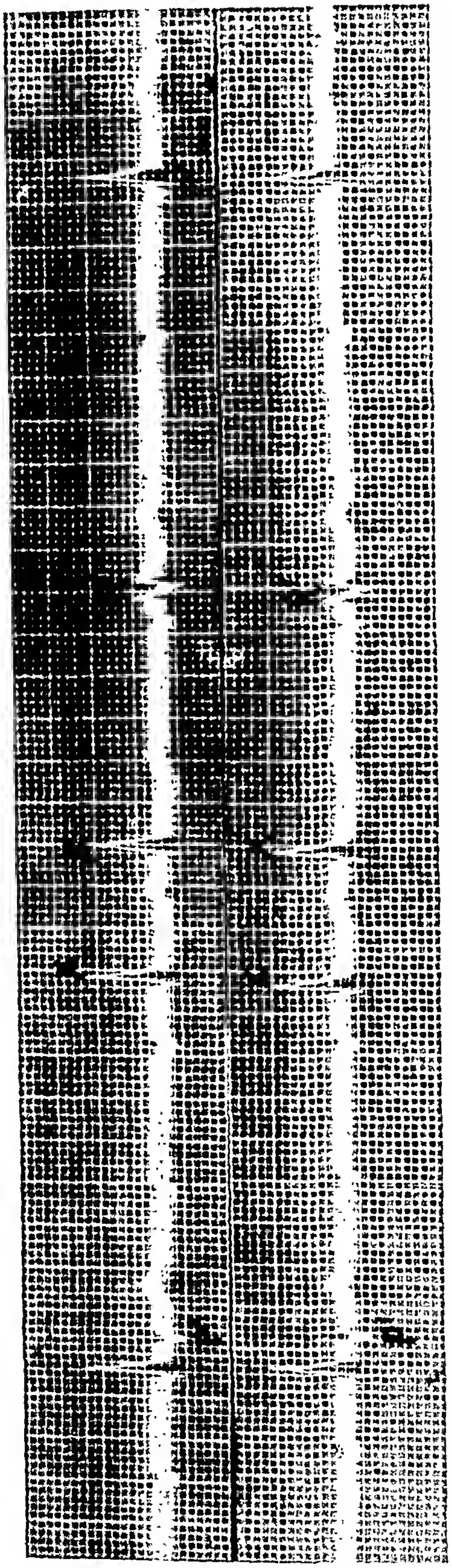

Fig. 11.—Case 3. The tracing shows that aberrant ventricular complexes in A-V sequences are not due to their slight prematurity since highly premature ventricular complexes have the normal form.

converted to 3-to-2, 2-to-1, or even 3-to-1 rhythm. An original 2-to-1 rhythm usually remained unchanged in spite of acceleration of auricular rate, although occasionally 3-to-1 rhythm resulted.

During periods of complete dissociation atropin sulphate in dosage of 3 mg. did not change the rhythm to the sequential type in either of two experiments. A third test was made when dissociation was almost but not quite complete (May 26, 1925), there being but occasional isolated sequential beats and a few short runs of 2-to-1 rhythm. Following the injection the usual auricular acceleration occurred and no more runs of 2-to-1 rhythm were observed although there were still isolated sequential beats.

These studies seemed to us to demonstrate beyond question that atropin showed no tendency to lessen block. Under its use the grade of block showed a tendency

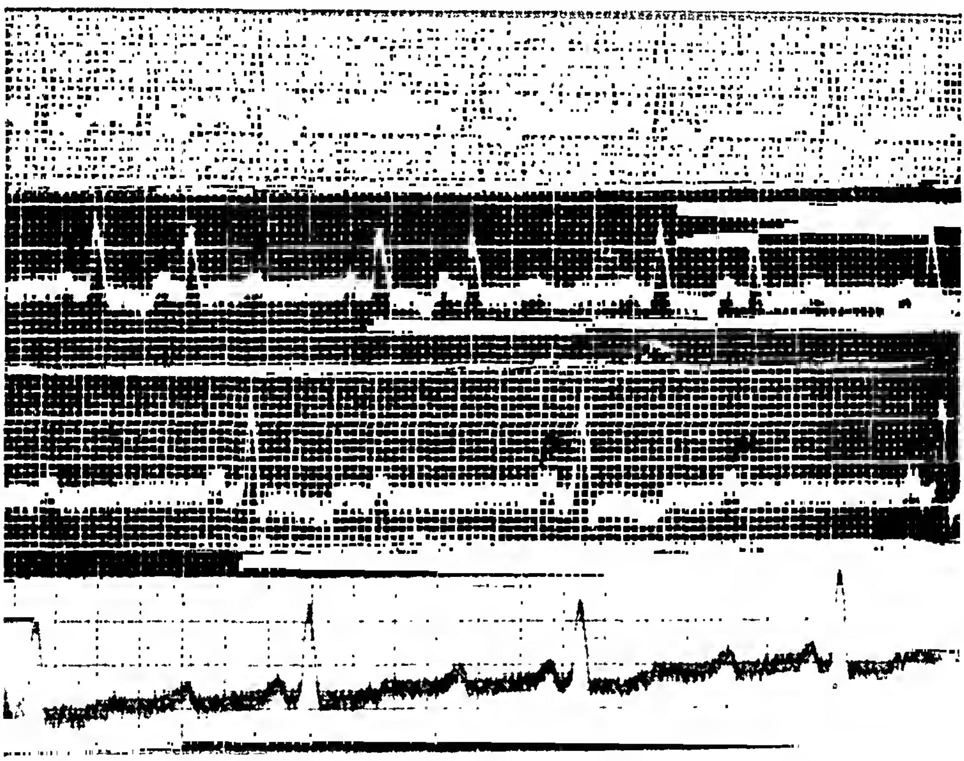

Fig. 12.—Case 3. Top strip shows end of a period of tachycardia in which there had been no block. Second strip shows 3-to-2 block; third strip, 2-to-1 block; and fourth strip, 3-to-1 block. All P-R intervals are well within normal limits. Such variations as are noted here occurred within periods of a few days.

to increase, probably due to acceleration of auricular rate rather than to any actual increased difficulty in conduction.

The effects of amyl nitrite are seen in Fig. 14. The effects seem to be quite identical with those of atropin except for the fact that they run their course over a period of a few minutes rather than hours. Like atropin the apparent increase in block is probably due merely to auricular acceleration.

Only one experiment was made with epinephrin because the drug caused very unpleasant pounding of the heart. On May 27, 1925, during a period of 2-to-1 rhythm intramuscular injection of 0.5 c.c. of a 1-1000 solution of epinephrin accelerated the auricular rate but failed to disturb the 2-to-1 rhythm.

The patient was rather intolerant of digitalis and nausea and vomiting tended to occur after 1 to 1.2 gram of digitan. Three experiments were made during periods of sequential beating in the attempt to convert the mechanism to com-

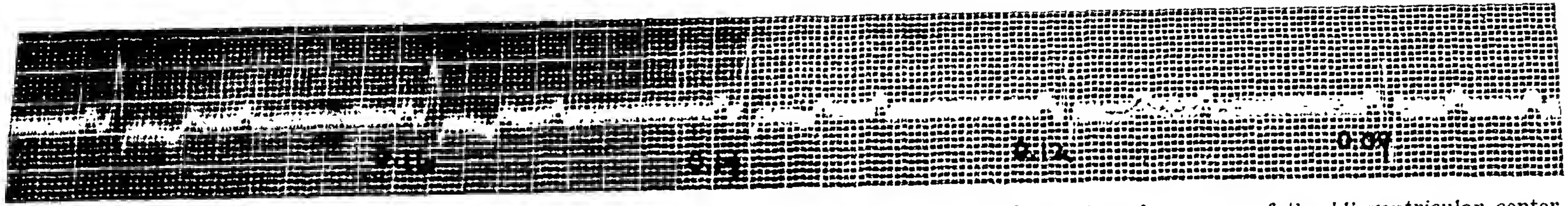

Fig. 13.—Case 3. Transition from *2-to-1* block to *idioventricular* rhythm. This is accomplished here by escape of the *idioventricular* center. Gradual change in *form* of ventricular complexes as the idioventricular center gradually gains control.

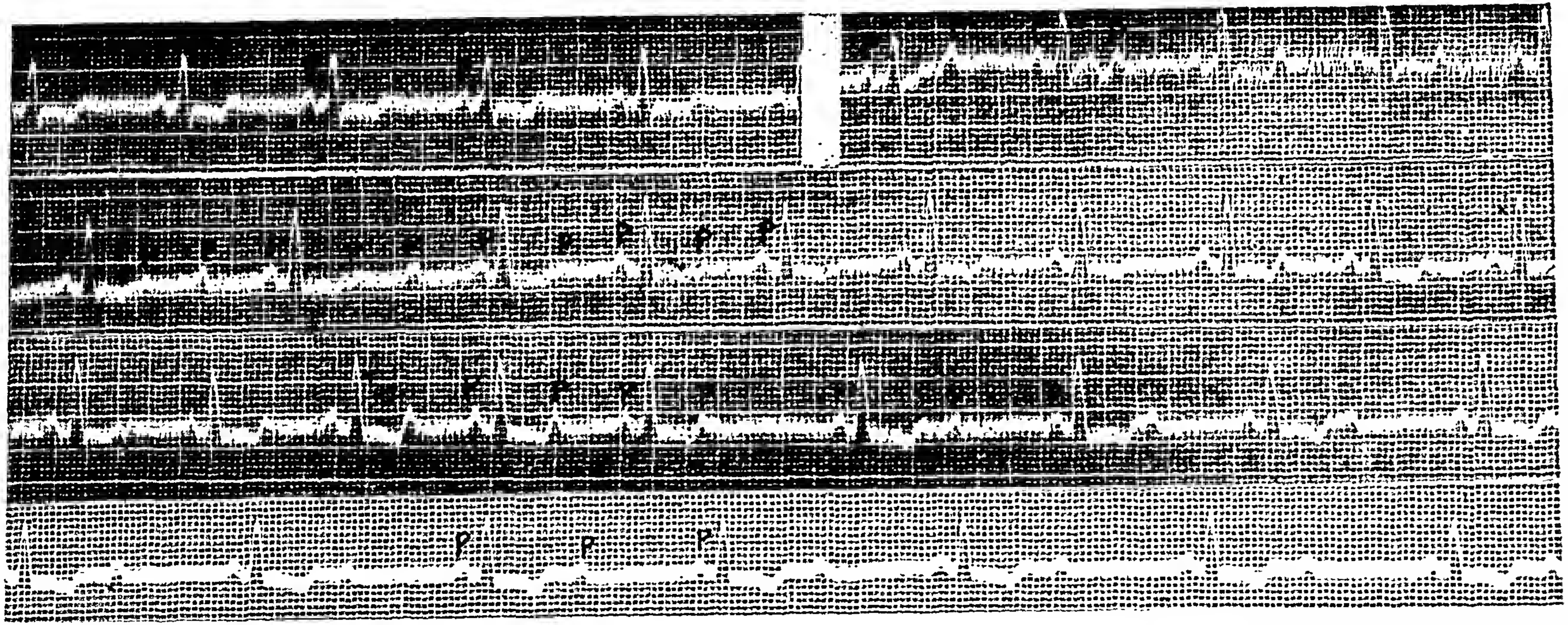

Fig. 14.—Selected strips of tracing before, during, and after amyl nitrite inhalation showing change from normal rhythm as the auricular rate *accelerated to* 2-to-1, then *3-to-1 block*. As the auricular rate began *to slow*, 2-to-1 block returned and persisted for a long time after the conclusion of the experiment. All P-R intervals are approximately constant and well within normal limits.

plete dissociation. The method used was administration by mouth of 0.13 gram of digitan t.i.d. to the point of vomiting which occurred on the third day. This occurred whether she did or did *not* know she was receiving digitalis. Twice no effect was noted on the sequential rhythm, but on the third attempt dissociation resulted about the time vomiting began. Because of the tendency to spontaneous change back and forth between sequential beating and complete dissociation, we did not feel justified in concluding that digitalis had been responsible for the change observed. The following morning after a few doses of barium chloride had been taken, there was 1-to-1 rhythm with no evidence of block. It therefore seemed possible that the shift to complete dissociation during this one of three trials with digitalis might have been accidental or at most evidence of a very feeble digitalis effect.

Barium chloride* was found for a long time to have a distinct effect in abolishing block and restoring 1-to-1 rhythm. Finally, however, it seemed to lose its effectiveness, at least in the dosage employed (20 mg., q.i.d.) We did not increase the dosage because of the production of ectopic ventricular beats singly and in series.

DISCUSSION

The Ventriculoauricular Sequential Beats.—A most instructive case has been reported by Krumbhaar[14] in which, despite the presence during life of complete heart-block, serial sections of the bundle showed comparatively little damage to the junctional tissues. In our Case 3 the presence of complete heart-block for quite some time before death suggested that complete destruction of the bundle at some point had occurred. Nevertheless, it was found that at the level of greatest damage approximately one-eighth of the bundle had apparently remained fairly intact. While these fibers had failed to transmit impulses for quite some time, probably several months, the histological findings suggested that there might have been ample muscle tissue present to conduct an impulse.

There is clinical evidence to indicate that complete block may be present for months without permanent loss of the ability to transmit impulses. One of us has observed a patient who showed complete heart-block in all examinations made during a period of six months but temporarily resumed normal rhythm with normal P-R intervals after eradication of extensive oral infection (unpublished case).

Findings of this type demonstrate the danger in assuming, because block has persisted for a relatively long time, that the ability to transmit impulses has been permanently lost. Furthermore, the assumption that if the ability to transmit impulses from auricles to ventricles is lost even transiently retrograde conduction must also be lost, is on equally uncertain ground. The possibility of unidirectional transmission cannot be excluded. Nevertheless on these foundations rests the reasoning which has led to the hypothesis of

*Studies of the action of barium chloride in this patient have been made the subject of a separate communication. (J. Lab. & Clin. Med. In Press.)

mechanical stimulation as the mechanism of retrograde beats in otherwise complete heart-block.

The data obtained in Case 3, so far as we are able to analyze it, offers no evidence in favor of mechanical stimulation of auricles by ventricles. It does, however, offer the following evidence in favor of retrograde transmission as the cause of the abnormal auricular beats although none of the points could be regarded as conclusive.

1. Retrograde sequences occurred only at such times as forward transmission was in evidence. If the retrograde sequences were due to mechanical stimulation, there would seem to be no good reason why they should not have occurred quite as readily at times when complete dissociation was established.

2. The P-R intervals and R-P intervals were approximately of the same length.

3. As in all other cases observed the R-P sequences occurred only in the latter part of the auricular cycles. The significance of this finding has been discussed above.

It seems to us, therefore, that the evidence we have been able to furnish in our three cases, supports in different ways the view that rapid retrograde sequences in the presence of high-grade or supposedly complete heart-block are due to retrograde conduction through the junctional tissues. It is opposed to the hypothesis of mechanical stimulation.* Furthermore the data supplied in connection with the cases previously published in support of the hypothesis of mechanical stimulation are not convincing.

Intermittent Heart-Block.—Wells and Wiltshire[15] have described a case in which intermittent complete heart-block was observed over a period of twelve years. Between attacks the transmission intervals were normal. At necropsy an area of calcification was found involving the A-V node, but continuity of muscle fibers in the bundle was apparently preserved.

In our Case 3 it is probable that intermittent complete block had lasted over a period as long as fourteen years although no electrocardiograms were made until five years before death.

Intermittent complete block is rare, and but few cases have been reported. The condition has been recently reviewed by Carter and Dieuaide[6].

Intermittent incomplete block with normal transmission intervals is not nearly so rare, and we as well as others have obtained records of a number of cases showing principally 2-to-1 block. The present

*We have failed in the attempt to force auricular contractions by mechanical stimulation from the ventricles in the dog. The method used was as follows: The dog was anesthetized by ether and an intratracheal respiration apparatus introduced. The thorax was opened, the pericardium incised, and a Lewis clamp applied to the junctional area so that complete heart-block was produced. Connection was then made between auricles and ventricles by means of a thread in the attempt to make a mechanical pull from the contracting ventricle to the auricle force auricular response. This was tried in many locations and with varying tensions of the thread but without success.

case shows the essential similarity in mechanism between intermittent incomplete and complete block, since numerous transitions occurred among normal rhythm, incomplete block with normal transmission intervals and complete block.

Carter and Dieuaide point out that there is indicated in intermittent complete block a progressive anatomical lesion of the auriculoventricular bundle and thus a tendency toward the establishment of permanent block. In this connection it is of interest to note in our Case 3 that the final period of complete block had probably lasted for several months preceding death and that the isthmus of relatively intact muscle in the bundle showing round-cell infiltration suggested progression in the lesion. Round-cell infiltration was also present in the bundle in Wells and Wiltshire's case.

It is possibly of some interest to speculate on the nature of a lesion that may permit sudden transitions back and forth between complete block and normal rhythm. Carter and Dieuaide's suggestion that the bundle contains only a few intact fibers which are just equal to the work of transmission under favorable circumstances but fail when stresses occur does not offer an explanation as to why in some cases of high-grade heart-block all transmitted beats have normal P-R intervals. The findings in our case suggest that the important factor may be the length of the critical area, in other words the distance through which the excitation must traverse damaged tissues.

Lewis[16] has proposed the view that prolongation of transmission intervals is due to the distribution of unexcitable tissue in the bundle in such a way as to require the excitatory process to pursue a sinuous course. Thus, if the barrier to conduction is short, it is easily conceivable that such impulses as are able to pass do so with little delay since little or no deflection from a straight course would occur.

Number and Condition of Fibers Capable of Conducting the Excitatory Process.—Factors which determine whether conduction or block of the excitatory process is to occur are not clearly understood. If the generally accepted view is correct, namely, that the excitatory process is an electrical disturbance transmitted from muscle fiber to muscle fiber, it would seem possible that continuity of single intact fibers might be sufficient to transmit the impulse effectively. It has been stated that a few fibers are capable of transmitting the impulse. Nevertheless, it is well known that conduction may fail despite the fact, that, as was shown in Krumbhaar's case,[14] later anatomical studies show abundant continuity of fibers which so far as can be told from their histological appearances should be capable of function.

Our Case 3 affords a very striking example of this apparent paradox. Transmission of the excitatory process frequently failed in the

main bundle, and during the last period of study before death transmission was not recorded despite the fact that serial sections of the bundle later showed that approximately one-eighth of the muscle was still present although doubtless somewhat damaged.

On the other hand, during periods of complete heart-block, the shape and duration of the QRS complexes of the electrocardiogram indicated that the impulses were spreading to the ventricles in a normal manner. From this we are compelled to assume that the impulse passed down not only the left main branch but also the right main branch as well. A tracing made three days before death still showed the normal type of QRS complexes. In spite of this finding the serial sections of the right branch showed that at one level destruction was complete except for a few atrophied fibers less than one-half the normal diameter. We must then conclude that these few greatly atrophied fibers conducted the excitatory process through the right main branch without appreciable delay. We are entirely unable to offer any explanation as to why on the one hand a mass of fibers relatively intact failed to function whereas a little lower a few greatly atrophied fibers apparently functioned normally. The natural inclination would be to question the data. Concerning the tracings there can be no question, and the sections have been studied so exhaustively as to seem to admit of no doubt as to correctness of the findings.

The Failure of Drugs and Vagus Stimulation to Effect the Degree of Block.—The response to atropin in the few cases of intermittent complete heart-block tested has been variable. In some previous cases it has been without effect. Carter and Dieuaide therefore repeat the previous warning of Lewis to the effect that atropin is not conclusive as to the pathogenesis of heart-block. In other words, the failure of atropin to relieve or decrease block does not exclude the possibility of a functional element being present, as opposed to anatomical loss of continuity in the bundle. This view our case abundantly confirms.

The description of our atropin experiments given above would seem to exclude the likelihood of vagus effect being concerned in the block. The most decisive experiment in this respect is regarded by us as the injection of atropin made when block was not quite complete. This should have been a peculiarly favorable time at which to demonstrate vagus effect yet none could be obtained.

The fact that during one-to-one transmission or various forms of incomplete block vagus stimulation was without effect in increasing block is further evidence of the absence of vagus effect. The uncertain or at most feeble effect of digitalis might also be interpreted as due in part to absence of vagus effect in the block.

The failure of amyl nitrite and our one experiment with epinephrin suggest that accelerator influences were also without effect.

From these experiments we conclude that nervous influences, either vagus or accelerator, were either entirely lost or so feeble as to be of no importance in the area of block.

It is of interest to note the effect of auricular rate on the grade of incomplete block. The results whether produced by amyl nitrite or by atropin were similar and may be seen in Fig. 14. As auricular rate was increased, there was a tendency for block to increase; and as the auricular rate declined, the grade of block declined. Thus in the course of a few minutes under the influence of amyl nitrite there was obtained 1-to-1, 2-to-1, 3-to-1, and 2-to-1 beating.

Barium chloride was the only drug which showed definite effect in abolishing block, although it finally lost its effect. Since barium is supposed to exert its effect by increasing excitability, we assume that this action was produced in the critical area. The final loss of this effect might have been due to the diminution of blood supply. An examination of the arterial twigs showed so much thickening and encroachment on the lumina of the vessels that the blood supply must have been precarious.

Aberrance of QRS Complexes of Sequential Beats.—Slight differences in shape between the ventricular complexes of idioventricular and transmitted beats are not uncommon. One of us has recently reported a case in which each type of beat has its characteristic QRS complex[17]. We have not, however, previously seen tracings in which the QRS complexes of transmitted beats were decidedly aberrant in form while those of idioventricular beats were within normal limits.

The degree of aberrance recorded in the ventricular waves of the transmitted beats is not sufficient to represent a complete bundle-branch block. It does, however, indicate some irregularity in the spread of the excitatory process through the ventricles. Nevertheless, the fact that idioventricular beats inscribe normal ventricular complexes suggested that the fault did not lie in either of the branches but was to be found above the idioventricular center.

The studies of the junctional tissues suggest that the explanation for the two types of ventricular curves is concerned with the position of the largest lesion. Fig. 9 shows that it lies mainly on the right side and dips into the right branch. Thus an impulse descending from above would have to traverse a slightly longer route to reach the right branch than the left and might, therefore, inscribe an aberrant QRS complex whereas an idioventricular beat arising in the bundle below the level of greatest destruction might be expected to have a more direct path to the right branch and therefore not be delayed appreciably in its spread to the right side.

SUMMARY

Cases previously reported exhibiting rapid retrograde sequences in the presence of high-grade heart-block have furnished no evidence regarding the mechanism of these sequences. We report three cases with somewhat different forms of behavior, all of which yield data bearing on this problem.

In Case 1 the duration of retrograde sequences is shown to be influenced by their proximity to other retrograde sequences.

In Case 2 the retrograde sequences occur in the presence of 2-to-1 heart-block. The auriculoventricular intervals are unusually long and the retrograde sequences less prolonged. A much shorter retrograde interval is observed following a long rest period. This case appears to furnish an instance of reciprocal beating, the excitatory process traveling from auricles to ventricles and then back to auricles.

In Case 3 isolated forward and retrograde sequences were recorded in short strips of tracing. The forward sequences exceeded in duration the retrograde sequences by about 0.01 second. After forward conduction ceased, retrograde sequences were no longer observed.

The phenomena observed in these three cases may be accounted for by the hypothesis that retrograde sequences in high-grade heart-block are due to retrograde transmission of the excitatory process through the area of block; they cannot be satisfactorily explained on the basis of mechanical stimulation of auricles by ventricles.

It is suggested that the association of high-grade heart-block with normal transmission intervals is due to a short critical area for conduction in the bundle. More serial sections of junctional tissues in cases of so-called intermittent heart-block are required to establish or disprove this view.

The functional capacity of junctional fibers to conduct the excitatory process does not always bear a close relationship to the histological appearance. Thus it was found in Case 3 that a few greatly atrophied fibers in the right branch functioned without delay while a much larger group of normal-appearing fibers in the main bundle failed to function.

Aberrations in QRS complexes short of complete bundle-branch block are not necessarily due to lesions below the branching of the main bundle. They may be caused by lesions in the lower part of the main bundle located in such a position that the pathway to one of the main branches is longer than the other.

Sudden apparently spontaneous changes among normal rhythm, incomplete, and complete block occurred in our Case 3 independently of demonstrable vagus or sympathetic nerve effects.

Our thanks are due to Dr. Edward B. Krumbhaar, Dr. Herbert Fox, and Dr. John Eiman for their expert advice and assistance in the preparation and study of the serial sections.

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ELECTROCARDIOGRAPHIC CHANGES IN DIPHTHERIA

I. Complete Auriculoventricular Dissociation*

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THERE is probably no acute disease in which changes in the circulatory system and cardiac mechanism occur as suddenly as in diphtheria. Such changes are among the most serious complications of the disease, and their importance is increased because of the fact that the medical profession is practically helpless in its efforts to prevent their occurrence or to remedy them after they have become evident. Further study of these effects in their various phases, therefore, seems justified.

This paper deals with the electrocardiographic observations on nineteen diphtheritic patients who developed complete auriculoventricular dissociation. Two distinct types of complete auriculoventricular dissociation occurring in diphtheria are described. Delayed P-R conduction preceding the onset of complete block is demonstrated. The frequent occurrence and probable causes of delayed QRS interval are discussed, and the striking similarity between the electrocardiographic abnormalities occurring in diphtheria and as a result of the toxic effects of digitalis is emphasized.

Several excellent studies of electrocardiographic observations in diphtheria have appeared in recent years. McCulloch[1] in 1920 observed 18 abnormal electrocardiograms in 80 consecutive cases of diphtheria. These vary from inverted T-waves to ventricular tachycardia, intraventricular conduction defects, bundle-branch block, and complete auriculoventricular block.

Smith[2] studied electrocardiograms from 242 consecutive cases of diphtheria. Simple tachycardia was the only abnormality observed in 72 per cent of his cases. Of the remaining cases, 65 per cent had sinus arrhythmia or sino-auricular block during convalescence. Premature contractions were present in 20 per cent, while 15 per cent of the remaining cases, or a little over 4 per cent of the total series, developed a high grade heart-block about the seventh day of the disease. The block was practically always of sudden onset and was followed by death within forty-eight hours in three-fourths of the cases; none of the patients recovered. Smith observed no instance of low grade heart-block. It is interesting to note that one of his patients resumed a normal mechanism, with the exception of markedly inverted T-waves, after complete heart-block but died suddenly the next day.

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Marvin[3] in an extensive survey of past writings, discussed the clinical, pathological, and electrocardiographic aspects of the problem and included an analysis of 90 patients of his own. He concluded that the only electrocardiographic abnormality of value in estimating cardiac damage or impending death is faulty conduction, either auriculo-ventricular or intraventricular. His autopsied cases showed varying degrees of myocarditis, at times including inflammatory changes of the conduction system. He described one case, suspected clinically of myocardial involvement, in which normal electrocardiograms were frequently obtained but which at autopsy showed marked myocarditis. The conduction system, histologically, was quite normal.

Parkinson[4] reported one patient with complete heart-block occurring in diphtheria, who is known to have recovered. Block was demonstrated by polygraph on the twenty-third day of the illness. Auricular fibrillation was noted four days later and was still present when the patient was seen six months later.

At least two instances of partial heart-block in diphtheria have been reported. Hume[5] published a polygraphic tracing showing 2-1 heart-block, and Marvin and Buckley[6] mention a similar case described by Hecht in which 2-1 heart-block persisted for four months and was followed by recovery.

Before analyzing the results of this study, a statement of each case is presented, with description of the electrocardiograms, and a brief summary of the cases is given in Table I.

TABLE I

CASE NO.	SEX	AGE	ANTITOXIN UNITS	ADMINISTRATION DAY OF DISEASE	DAY OF DISEASE BLOCK WAS DISCOVERED	DURATION OF OBSERVATION OF BLOCK
1	F	15	20,000	4th day	10th day	4 days
			40,000	7th day		
2	M	5	40,000	6th day	7th day	Less than one day
3	F	8	40,000	3rd day	7th day	Less than one day
4	M	4	40,000	4th day	8th day	Less than one day
5	F	2	None		Unknown	4 days
6	F	5	40,000	4th day	8th day	Less than one day
7	F	5	20,000	2nd day	6th day	2 days
			20,000	6th day		
8	M	14	40,000	5th day	12th day	5 days
9	M	7	40,000	6th day	10th day	1 day
10	F	5	40,000	3rd day	8th day	4 days
11	M	5	Unknown	5th day	10th day	Less than one day
12	M	13	40,000	4th day	5th day	4 days
13	F	6	20,000	3rd day	11th day	Less than one day
			40,000	6th day		
14	M	7	10,000	2nd day	10th day	1 day
			10,000	4th day		
15	F	2	45,000	4th day	9th day	3 days
16	F	3	10,000	3rd day	7th day	4 days
			10,000	5th day		
17	M	9	40,000	7th day	9th day	1 day
18	F	18	40,000	5th day	7th day	10 days
19	M	10	Unknown	7th day	10th day	Less than one day
			40,000	10th day		

CASE REPORTS

CASE 1.—A white girl, 15 years old, received 20,000 units of antitoxin on the fourth day, and 40,000 units on the seventh day. The electrocardiogram of the seventh day shows a normal mechanism with a rate of 130, left ventricular preponderance and T-wave in the opposite direction to the main ventricular deflection in Leads II and III. A record taken on the tenth day shows complete heart-block,

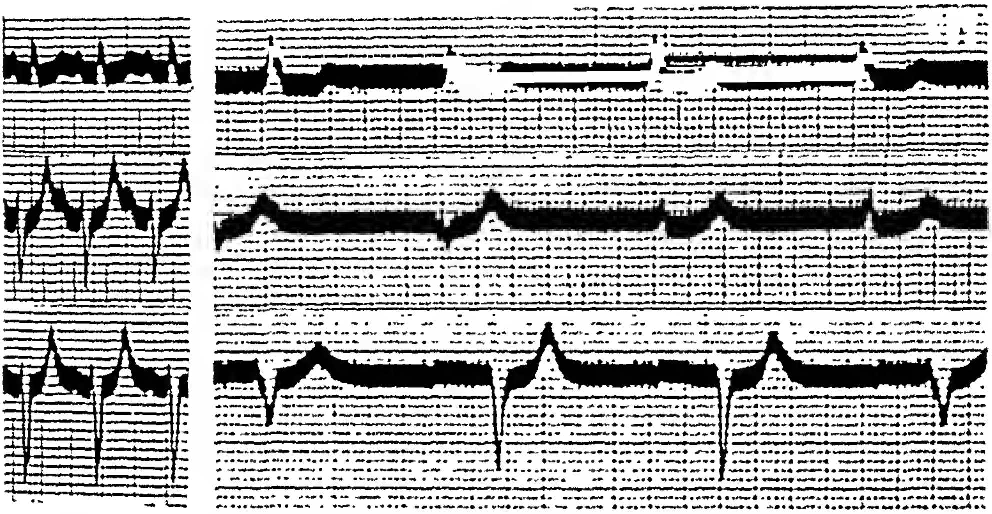

Fig. 1.—From Case 1. The first part is a record taken on the seventh day of disease showing normal mechanism, simple tachycardia of 130, and left ventricular preponderance. The T-waves in Leads II and III are opposite in direction to the main ventricular deflection. The second part was taken on the tenth day of disease and shows complete heart-block with an auricular rate of 80 and ventricular rate of 50, both slightly irregular. There is left ventricular preponderance, QRS interval of 0.12 second, variation of ventricular complexes and T-waves opposite in direction to main ventricular complexes in Lead III.

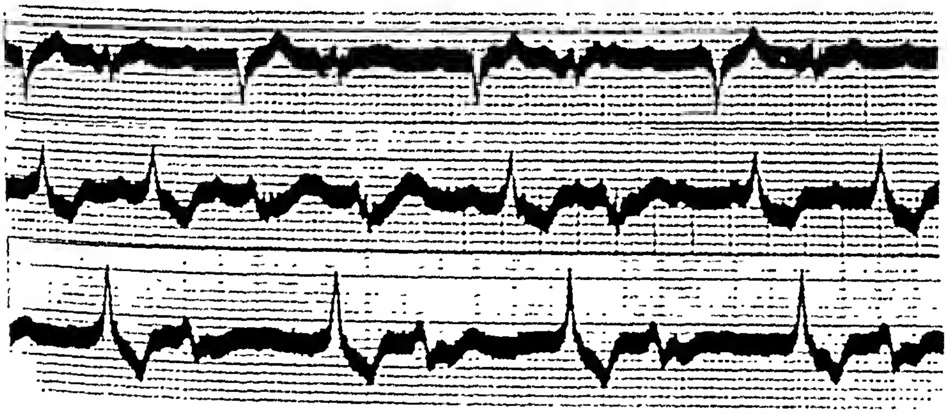

Fig. 2.—From Case 1, taken on the twelfth day of disease. Record shows complete heart-block with auricular rate of 200 and ventricular rate of about 90. There is coupled rhythm in Leads I and III, right ventricular preponderance and T-waves are in opposite direction to the main ventricular complexes.

QRS interval of 0.12 second, left ventricular preponderance, and variation in the ventricular complexes (Fig. 1). The auricular rate is 80 and the ventricular 50, both slightly irregular. On the twelfth day there is a definite coupled rhythm in Leads I and III, right ventricular preponderance, an auricular rate of 200, and a ventricular rate of 90, the latter slightly irregular because of the coupled rhythm (Fig. 2). Death occurred on the thirteenth day.

CASE 2.—A white boy, 5 years old, received 40,000 units of antitoxin on the sixth day. An electrocardiogram taken on the seventh day of the disease shows complete heart-block with a ventricular rate of 163 and an auricular rate of 155. The ventricular complexes are essentially normal except for a delay in the QRS interval

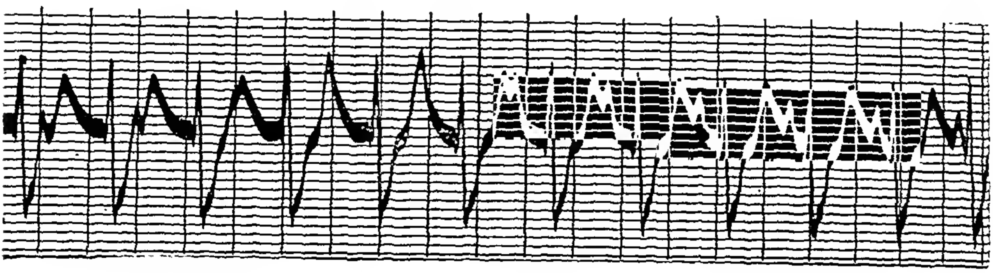

Fig. 3.—From Case 2. Lead II of a record taken on the seventh day of the disease showing complete heart-block with auricular rate of 155 and ventricular tachycardia of 163. There is right ventricular preponderance and delayed QRS interval of 0.12 second. P-waves are easily recognizable.

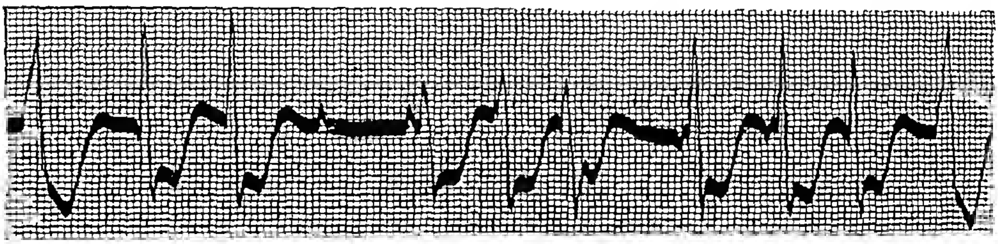

Fig. 4.—From Case 3. Lead II of a record taken on the seventh day showing complete heart-block. The auricular rhythm is fairly regular with a rate of 110. P-waves are prominent but frequently change their form. Ventricular rhythm is irregular with a rate of about 120. Complexes vary in Leads II and III, and there is right ventricular preponderance.

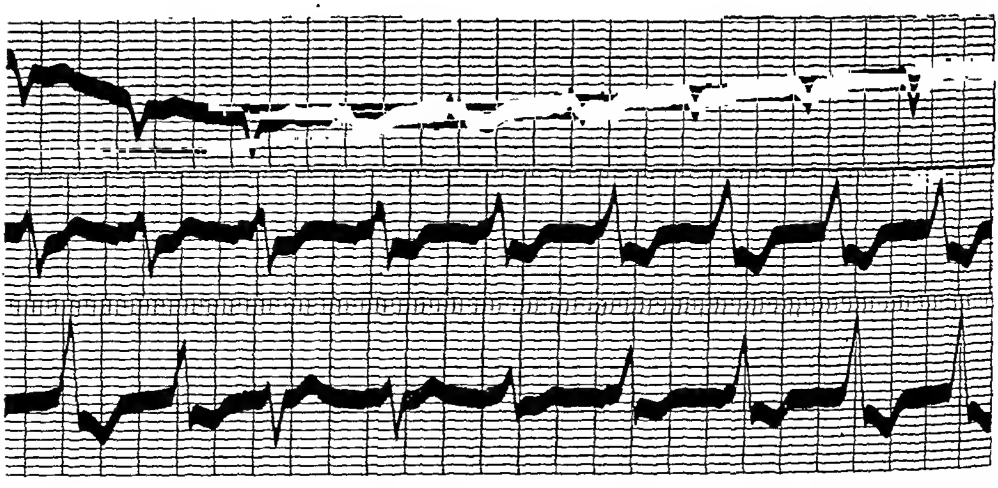

Fig. 5.—From Case 4. Record taken on the eighth day of the disease showing complete heart-block with auricular rate of 90 and ventricular rate of 100. The ventricular complexes vary gradually from positive to negative. QRS interval varies from 0.12 to 0.16 second, and T-wave is always in opposite direction to main ventricular deflection.

to 0.12 second. There is right ventricular preponderance, and T-waves are opposite the main ventricular deflection (Fig. 3). Death occurred shortly after this record was taken.

Case 3.—A white girl, 8 years old, received 40,000 units of antitoxin on the third day of the disease. An electrocardiogram taken on the seventh day shows complete heart-block with cardiac action due entirely to short runs of ventricular tachycardia, varying from 3 to 11 beats. QRS interval varies from 0.1 to 0.12 second. The ventricular complexes vary in shape, and ventricular rhythm is irregular with a rate of 120. Definite P-waves are distinguishable, but nowhere do they seem to stimulate ventricular contraction. The P-waves change their form,

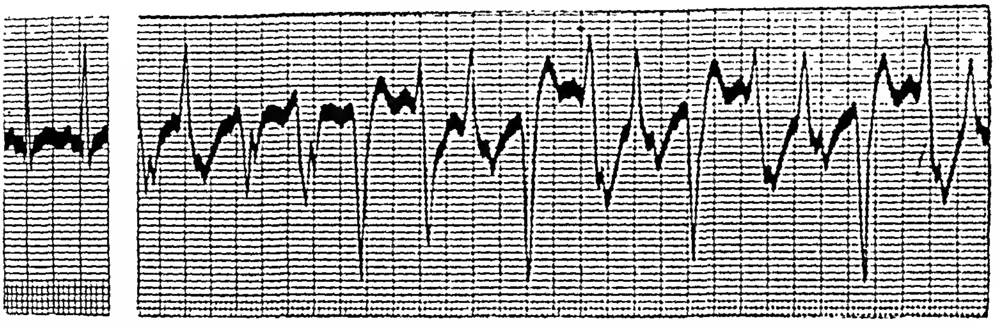

Fig. 6.—From Case 6. First record, taken on the eighth day of disease, shows normal mechanism, right ventricular preponderance, and simple tachycardia of 136. The second record, taken four hours later, shows rapid and irregular ventricular tachycardia with bizarre and rapidly changing ventricular complexes, which at times are alternating. QRS interval varies but at times is 0.2 second. P-waves are not recognizable.

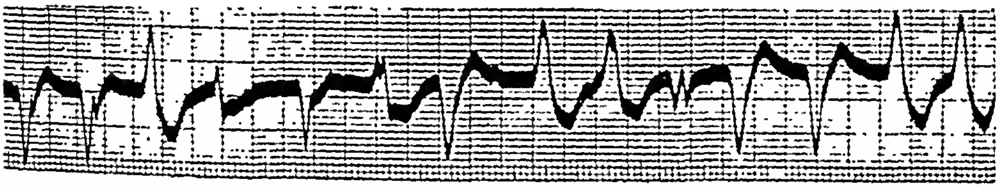

Fig. 7.—From Case 7. Record taken on the eighth day of disease shows an irregular ventricular tachycardia of about 130 The ventricular complexes vary in shape, at times alternate in direction and QRS interval is definitely prolonged.

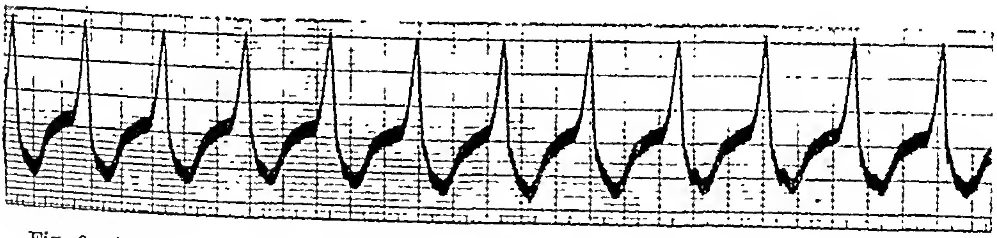

Fig. 8.—From Case 7, taken the day after Fig. 7. Record shows a regular ventricular tachycardia of 120, right ventricular preponderance, and delayed QRS interval of 0.16 second. Auricular rhythm is regular with a rate of 113.

and the auricular rhythm is fairly regular with a rate of 110 (Fig. 4). Death occurred on the seventh day.

Case 4.—A white boy, 4 years old, received 40,000 units on the fourth day of the disease. An electrocardiogram taken on the eighth day shows complete block with a fairly regular ventricular rate of about 120. The auricular rate cannot be distinguished. A record of the following day shows the same block and also intraventricular block, with complexes gradually varying from positive to negative in all leads. QRS interval is prolonged, being from 0.12 to 0.16 seconds. The ventricular rate is 100, and auricular rate 90, both regular (Fig. 5). The patient died the same day.

CASE 5.—A white girl, 2 years old. The date of onset is not definitely known but was about three weeks before entry. The patient developed paralysis of the palate one week before entry. A record taken four days after entry shows complete heart-block, ventricular rate of 140, auricular rate 100, both regular. Ventricular complexes are normal except for low voltage. Death occurred five days after admission to the hospital.

CASE 6.—A white girl, 4 years old, received 40,000 units of antitoxin on the fifth day of the disease. An electrocardiogram taken on the eighth day is normal except for a tachycardia of 136. A record four hours later shows rapid and irregular ventricular tachycardia of 140 with rapidly changing ventricular complexes, which at times are alternating. P-waves are not distinguishable. QRS interval varies but is markedly prolonged to 0.2 seconds (Fig. 6). Death occurred within an hour of this record.

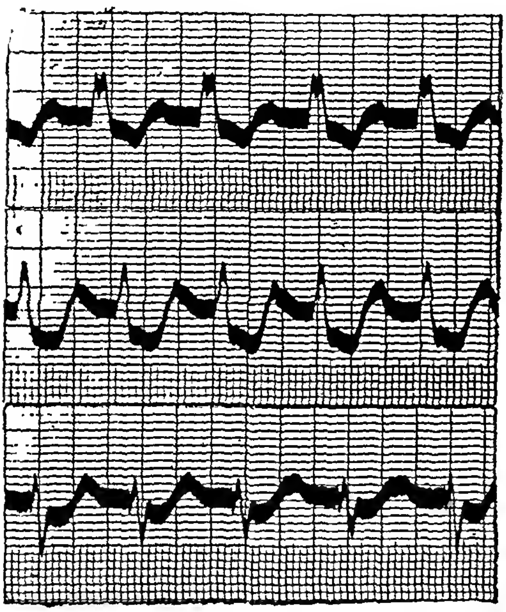

Fig. 9.

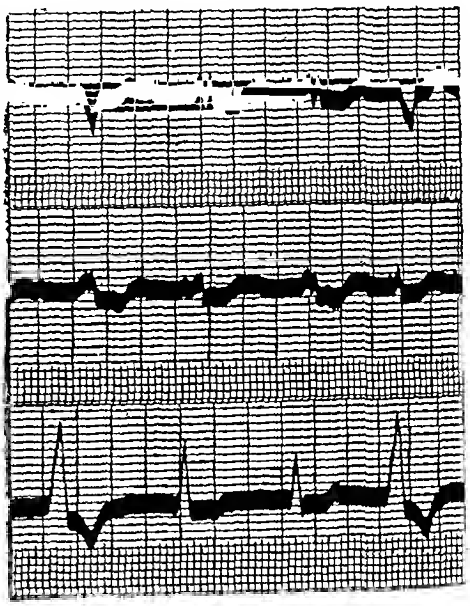

Fig. 10.

Fig. 9.—From Case 9. Record, taken on the seventh day of the disease, shows tachycardia of 100, delayed P-R conduction of 0.22 second, prolonged QRS interval of 0.12 second and T-waves in opposite direction to main ventricular deflection.

Fig. 10.—From Case 9. Record taken on the tenth day shows complete heart-block, with auricular rate of 140 and ventricular rate about 90. There is right ventricular preponderance, the ventricular complexes vary markedly and QRS interval is prolonged. In Lead III, T-waves vary from upright to downward in spite of the fact that the ventricular complexes are all upright.

CASE 7.—A white girl, 5 years old, received 20,000 units of antitoxin on the second day of the disease and also on the sixth day of the disease. An electrocardiogram taken on the seventh day shows ventricular tachycardia and complete heart-block, with impulses arising regularly in the right ventricle. The auricular rate is 150 and the ventricular rate 120. A record on the following day shows an irregular ventricular tachycardia of 130, with rapidly changing, bizarre ventricular complexes. The auricular rate is 110 (Fig. 7). On the ninth day, the day of death, the heart again became regular, and the tracing resembles closely the one taken two days before. The auricular rate is 113 and the ventricular rate 120 (Fig. 8). QRS interval varies but is definitely prolonged to 0.16 second.

CASE 8.—A white boy, 14 years old, received 40,000 units of antitoxin on the fifth day of the disease. An electrocardiogram taken on the twelfth day shows complete dissociation and an irregular mechanism interpreted as a ventricular tachycardia. The auricular rate is 100 and the ventricular 120. Two days later an essentially similar record was obtained in which the ventricular rate is 140; the auricular rate cannot be distinguished. QRS interval in both records is definitely prolonged. Death occurred on the seventeenth day.

CASE 9.—A white boy, 7 years old, received 40,000 units of antitoxin on the sixth day of the disease. An electrocardiogram taken on the seventh day shows a normal mechanism with delayed P-R conduction of 0.22 second. The QRS interval is about 0.12 second, the R-wave is splintered in Lead I, and the T-wave is opposite in direction to the QRS in all leads (Fig. 9). A record taken on the tenth day shows complete dissociation with a regular auricular rate of 140 and an irregular ventricular rate of 90. Ventricular complexes vary markedly, QRS interval is prolonged, and in Lead III the T-wave at times is inverted and at times

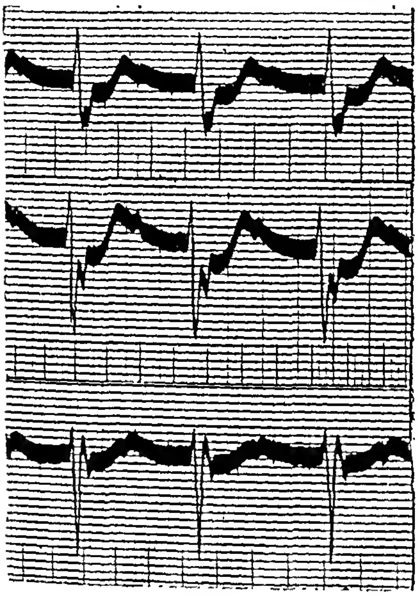

Fig. 11.

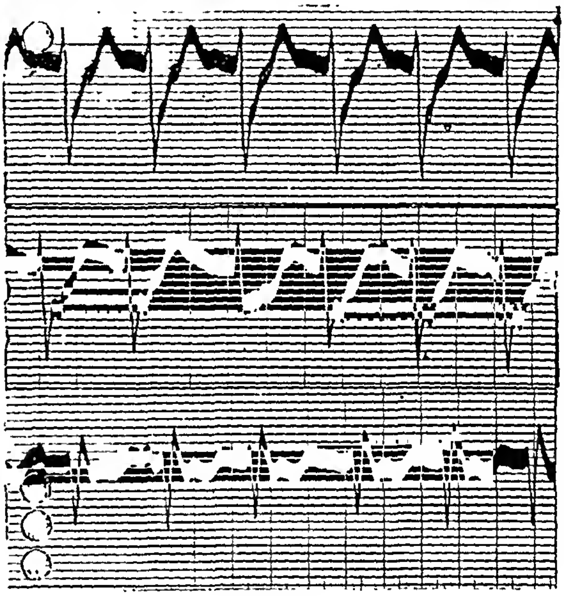

Fig. 12.

Fig. 11.—From Case 10. Record taken on the eighth day shows delayed P-R conduction of 0.36 second. There is marked left ventricular preponderance and prolonged QRS interval. The rhythm is regular and rate 80.

Fig. 12.—From Case 10. Record taken the day after Fig. 11 shows complete heart-block with auricular rate of 110 and ventricular rate of 120, the latter being somewhat irregular. QRS interval is 0.12 second.

upright, in spite of the fact that the QRS complexes are all upright (Fig. 10). Death occurred the following day.

CASE 10.—A white girl, 5 years old, received 40,000 units of antitoxin on the third day. Electrocardiograms taken on the seventh and eighth days of the disease show nodal rhythms and rather bizarre complexes and rates of 110 and 100 respectively. A record taken six hours later shows ventricular complexes which are essentially unchanged, but P-waves are distinguishable, the P-R interval is 0.36 second, and the rate has dropped to 80. The S-wave is splintered in Lead II, and T-waves are in opposite direction to the main ventricular deflection (Fig. 11). In a record of the following morning there is complete dissociation with an auricular rate of 110 and a ventricular rate of 120, both regular. The third complex in Lead II differs from the others (Fig. 12). QRS interval is 0.12 second in both of these records. Death occurred on the eleventh day.

CASE 11.—A white boy, 5 years old, received antitoxin on the fifth day, but the amount is unknown. He entered the hospital on the tenth day with a diagnosis of dilatation of the heart and died several hours after admission. The electrocardiogram shows a fairly regular ventricular rhythm with rate of about 60. P-waves are small but at times indistinguishable so that the auricular rate cannot be determined. There is marked widening of the QRS interval to almost 0.2 second. The ventricular complexes vary markedly in height in Lead III, and the T-waves are opposite in direction to the main ventricular deflection in all leads.

CASE 12.—A white boy, 13 years old, received 40,000 units of antitoxin on the third day of the disease. On the fifth day the pulse rate dropped to 65. An electrocardiogram taken at this time shows complete heart-block, low voltage, slight delay in QRS interval of 0.1 second, an auricular rate of 118, and ventricular rate of 66, both regular. Death occurred on the eighth day.

CASE 13.—A white girl, 6 years old, received 20,000 units of antitoxin on the third day of the disease and 40,000 units on the sixth day. An electrocardiogram

Fig. 13.—From Case 13. Record shows complete heart-block and alternating bidirectional ventricular rhythm. The auricular and ventricular rates are about 80, but the P-R interval varies markedly. QRS interval is prolonged to 0.16 second at times. T-waves are in the opposite direction to main ventricular deflections.

taken on the day of death, which was the eleventh day of the disease, shows complete heart-block with a slightly irregular ventricular rate of 160. P-waves are distinguishable but occur rather irregularly. QRS interval is about 0.1 second.

CASE 14.—A white boy, 7 years old, received 10,000 units of antitoxin on the second and fourth days of the disease. An electrocardiogram taken on the tenth day of the disease shows complete heart-block with slightly irregular ventricular rate of 126 and an auricular rate of 100. Ventricular complexes vary slightly but are essentially normal except for QRS interval of 0.12 second. Death occurred the following day.

CASE 15.—A white girl, 2 years old, received 45,000 units of antitoxin on the fourth day of the disease. The pulse rate varied from 100 to 140 until the ninth day when it fell to 50. An electrocardiogram taken on the tenth day shows complete heart-block with an auricular rate of 100 and a ventricular rate of 40,

both regular. There is left ventricular preponderance, and QRS interval varies from 0.12 to 0.16 second. A record of the eleventh day shows the same. Death occurred on the twelfth day.

CASE 16.—A white girl, 3 years old, received 10,000 units of antitoxin on the third and fifth days. An electrocardiogram taken on the seventh day shows complete heart-block, marked variation in the ventricular complexes, ventricular rate of 110 somewhat irregular, and an auricular rate which could not be determined. Another record taken two days later shows complete heart-block with fairly normal ventricular complexes except for low voltage, a ventricular rate of 97 and auricular rate of 136, both regular. Death occurred on the eleventh day.

CASE 17.—A white boy, 9 years old, received 40,000 units on the seventh day of the disease. An electrocardiogram taken on the ninth day shows complete auriculoventricular dissociation, delayed intraventricular conduction of from 0.12 to 0.17 second, inverted T-waves, regular rhythm, ventricular rate of 90, and an auricular rate of 126. QRS complexes are upright in all leads. Death occurred on the tenth day.

CASE 18.—A white girl, 18 years old, received 40,000 units of antitoxin on the fifth day of the disease. On the seventh day the pulse fell to 60, and a record showing complete heart-block was obtained. From this day until death, on the seventeenth day, sixteen tracings were made. All show complete auriculoventricular dissociation varying from regular to irregular and in rate from 60 to 140. There is marked variation in ventricular complexes and in QRS intervals up to 0.16 second. Alternating bi-directional ventricular rhythm is seen twice (Fig. 13).

CASE 19.—A white boy, 10 years old, received two doses of antitoxin from the seventh to the tenth day of the disease, at which time he entered the hospital and was given 40,000 units in addition. On entrance the patient was pale and pulseless; heart was dilated and irregular. An electrocardiogram shows complete auriculoventricular dissociation with irregular rhythm and varying ventricular complexes, also marked delay in QRS conduction up to 0.2 second. Death occurred four hours after entry.

DISCUSSION

This study is based upon observations of all cases of clinical diphtheria in which the presence of complete heart-block was proved electrocardiographically. In no instance was resumption of a normal rhythm observed following the institution of block. These patients were all under twenty years old, and in every instance death occurred in from a few hours to ten days following the appearance of complete heart-block. All except one received substantial doses of diphtheria antitoxin, some as early as the second, third and fourth days of the disease. The duration of the disease before the observation of block varied from six to twelve days. In one case this period was unknown.

There are at least two ways in which complete auriculoventricular dissociation may occur. One is disfunction of the A-V bundle itself, manifested first as a delayed P-R interval, then presumably by a period of dropped beats, and finally a complete block with an independent but slow ventricular rhythm. This may be the result of an actual organic involvement of the conduction system.[3] The other way is by a func-

tional disarrangement, probably caused by toxins, without irreparable damage to the conduction system, as evidenced by the case reported by Smith,[2] in which a normal rhythm returned after complete heart-block. This would indicate that anatomical destruction of the conduction system is not necessary for the production of block. Chloroform and digitalis poisoning and asphyxia cause other toxic states which may be associated with heart-block, but in which recovery is not uncommon.

Complete auriculoventricular dissociation also occurs as a result of increased irritability of the ventricular muscle from various poisons which set up an independent rhythm in the ventricles, i.e., a ventricular tachycardia with a rate faster than that of the sinus or the auricles. Under these conditions dropped beats are not to be expected. This augmented irritability is often associated with defective intraventricular conduction, shown by prolonged QRS interval and rapidly changing

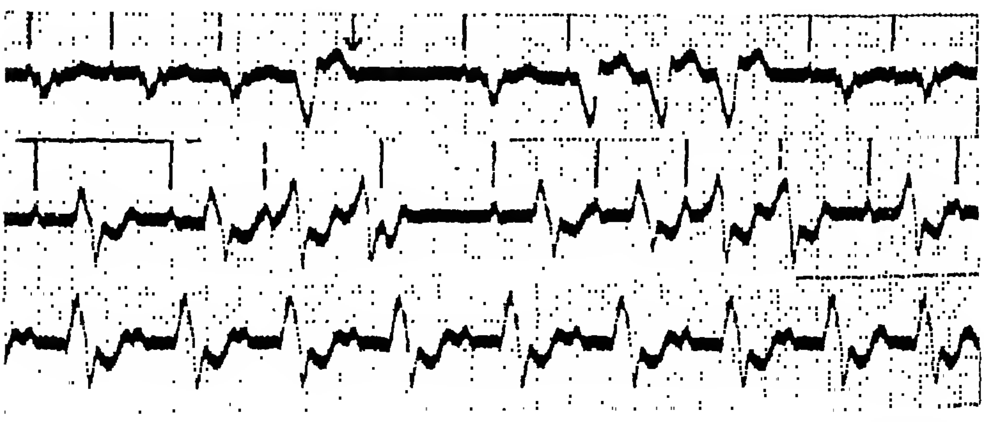

Fig. 14.—Record from a case not included in this series because complete heart-block was not observed. The solid lines point to definite P-waves, the broken lines to probable P-waves and the arrow in Lead I to a dropped beat. P-R interval is 0.26 second when it is recognized, ventricualr escape is common, the ventricular rhythm is irregular, and QRS interval is 0.18 second. The auricular rhythm is very irregular and at times seems to disappear for short periods.

form of ventricular complexes from beat to beat. White[7] described two methods by which the ventricular rate exceeded the auricular rate. One occurs when the automatic stimulus production in the atrioventricular node is released by any factor which depresses and slows the sino-auricular node; the other, which he characterizes as a rare type, occurs when the atrioventricular node becomes so irritable as to escape from control of the sino-auricular node. He described three cases of his own and several from the literature, three of which were apparently due to digitalis and one to strophanthus. After large doses of atropine Wilson[8] saw this phenomenon during forced respiration. Christian[9] reported four cases showing varying degrees of block and rapidly changing form of ventricular complexes which he attributed to digitalis administration. Hewlett and Barringer[10] point out that digitalis first decreases the heart rate but later causes independent auricular and

ventricular rhythms. Under these circumstances the ventricular rate approaches or exceeds the auricular rate. They report a clinical case of this kind in which the patient died twenty-four hours after onset. Heard and Colwell[11] cite a case of permanent block of the right bundle-branch with transient periods of complete auriculoventricular dissociation which were definitely related to digitalis administration. In most of these periods the ventricular rate exceeds the auricular rate.

It seems surprising that minor grades of heart-block are not more frequently encountered in diphtheria. From observations of cases on which many electrocardiograms were made, it is evident that profound changes in cardiac function occur very rapidly. Three records, however, are shown in which the P-R interval is definitely abnormal. In Case 9 (Fig. 9) the P-R interval is prolonged to 0.22 second with a regular rhythm and a rate of 100. Three days later there is complete block with an auricular rate of 130 and ventricular rate of 90 (Fig. 10). In Case 10 (Fig. 11) P-waves are definite and P-R interval is

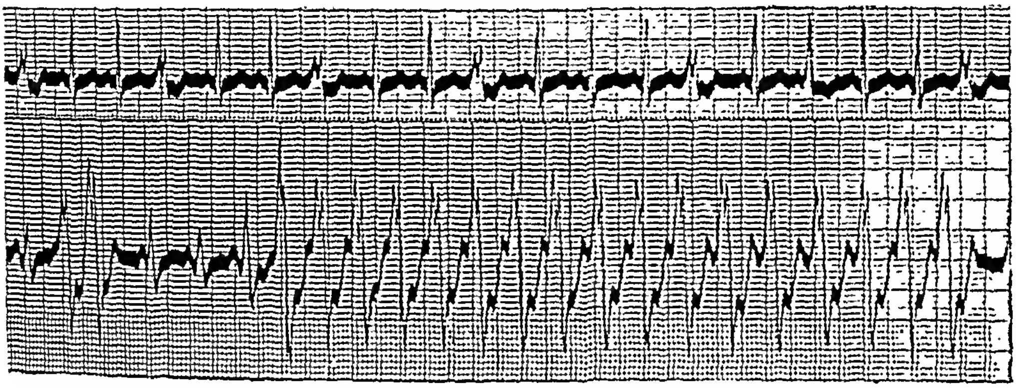

Fig. 15.—Record from a case not included in this series. Lead I shows normal mechanism except for frequent extrasystoles. Lead III shows extrasystoles and one short run of ventricular tachycardia with rate of 180. The patient made an uneventful recovery.

markedly prolonged to 0.36 second with a regular rhythm and rate of 80. On the following day there is complete block with an auricular rate of 110 and a ventricular rate of 120 (Fig. 12). The third record is from a case not included in this series because complete heart-block is not demonstrated (Fig. 14). Ventricular complexes are bizarre in shape; QRS interval is markedly prolonged to 0.18 second. Ventricular escape is common in Leads I and II; but where ventricular complexes follow P-waves, the P-R interval is 0.26 second. The wave marked in Lead I represents a dropped beat. Both auricular and ventricular rhythms are irregular.

Ventricular tachycardia in diphtheria may be a transient disorder and is not necessarily fatal. For example, Fig. 15 is a record taken from a patient not included in this series, but who showed this transient disorder from which he promptly recovered. In this record ventricular extrasystoles are common, and a few runs of ventricular

tachycardia occur; but conduction is not seriously impaired because normal conduction sequence prevails. It is interesting to compare this with Fig. 4 in which only short runs of extrasystoles are seen. In this figure there are several pauses as long as one second containing well-marked P-waves but normal ventricular complexes do not follow. Auriculoventricular conduction does not occur.

The individual records of ventricular tachycardia in this series show marked degrees of variation in rhythm. Some are quite regular, as described in Cases 2, 5, 7, 8, 10, 12, 15 and 17 (Figs. 4 and 8); some show a gradual but rhythmical change as in Case 4 (Fig. 5); while still others show rapidly changing and wildly bizarre complexes, as in Cases 6 and 7 (Figs. 6 and 7), and to a slighter extent in Case 9 (Fig. 9).

Alternating bi-directional ventricular tachycardia can be found in Cases 6 and 7 (Figs. 6 and 7), lasting only during several beats. Case 18 (Fig. 13), however, exhibits a ventricular rhythm with alternating complexes in opposite directions for a considerable period. This phenomenon is observed in two records taken six hours apart, after which it changes to a regular ventricular rhythm arising in the right ventricle. Alternating bi-directional ventricular rhythm was first described by Schwensen.[12] Palmer and White[13] reviewed the literature in 1928, finding only thirteen cases illustrating this phenomenon. Six months later Marvin[14] reported five additional examples. All of these were cases of middle-aged patients with damaged and fatigued myocardia, who had received substantial or excessive doses of digitalis. The authors believe that this drug constituted the most striking etiological factor. This represents a serious cardiac condition, as death usually occurred in several days.

Prolongation of the QRS interval is one of the most constant changes of the ventricular complexes in this series. In fourteen cases it varied from 0.12 to 0.2 second. In two cases it was 0.1 second, the upper limit of normal; while in only two cases (Cases 5 and 16) was it under 0.1 second. Prolongation of the QRS complex has been attributed in part to dilatation of the heart with resultant lengthening of the conduction paths. While this may contribute, it seems inconceivable that the paths of conduction can be increased to two and three times their normal length. It appears more likely that toxic depression in diphtheria impairs conduction. That this actually occurs is shown in the following article of this series by demonstrating electrocardiographic tracings of patients with marked QRS prolongation and even bundle-branch block followed shortly by clinical and electrocardiographic recovery. Wilson and Herrmann[15] reported a case of uremia in which the QRS interval increased to 0.2 second on the day of death. They attributed this to a toxic depression of the conductivity of the Purkinje system. In his studies of the toxic rhythms due to digitalis, Luten[16] states that digitalis is known to depress intraventricular conduction.

In another article[17] he says, "Our patients who exhibited signs of severe toxemia and at the same time showed independent ventricular rhythm gave records which contained also evidence of impaired intraventricular conduction." Robinson,[18] on the other hand, reports cases in which prolongation of the QRS interval was decreased when clinical improvement occurred as a result of rest and digitalis.

Though none of the patients of this series received digitalis medication of any sort during their stay in the hospital, the electrocardiographic changes show a striking similarity to some of the toxic effects of digitalis. Of the evidences of toxicity, prolonged P-R coduction has been pointed out in Cases 9 and 10 (Figs. 9 and 10). Complete heart-block with slow ventricular rhythm occurred in Cases 1, 11, 12, and 15 (Fig. 1). A striking coupled rhythm quite similar to that seen as a digitalis effect is shown in Case 1 (Fig. 2). Of the less frequently seen but well-known disorders following digitalis are ventricular tachycardia with a ventricular rate faster than the auricular rate in Cases 2, 5, 7, 8, and 10 (Figs. 3, 8, and 12), irregular ventricular tachycardia in Cases 3, 4, 7, 9, 12, 13, 14, 16, and 18 (Figs. 4, 6, and 7), varying and bizarre ventricular complexes in Cases 1, 3, 4, 6, 7, 9, 16, 18, and 19 (Figs. 1, 5, 6, 7, and 10), delayed QRS conduction in Cases 1, 3, 4, 6, 7, 8, 9, 10, 11, 14, 15, 16, 17, 18, and 19 (Figs. 1, 2, 4, 5, 6, 7, 8, 9, 10, 12, and 13), and alternating bi-directional ventricular tachycardia in Cases 6, 7, 18, and 19 (Figs. 6, 7, and 13). This supports the experience of pediatricians that digitalis is definitely contraindicated in diphtheria.

SUMMARY

1. Nineteen cases of complete heart-block occurring in diphtheria were studied electrocardiographically. All terminated fatally.

2. Heart-block in diphtheria probably results from a toxic action upon the conduction system which renders it functionally inactive or from an irritation of the ventricular muscle which results in the setting up of an independent ventricular rhythm with a rate faster than that of the auricles. Both effects may occur simultaneously.

3. Some of the effects of diphtheria on the cardiac mechanism simulate closely the toxic effects of digitalis.

4. The opinion that digitalis is contraindicated in diphtheria is substantiated.

The author wishes to express his appreciation to Dr. J. A. Toomey and the Department of Contagious Diseases for permission to study these cases.

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VENTRICULAR FIBRILLATION: ITS RELATION TO HEART-BLOCK

Report of a Case in Which Syncopal Attacks and Death Occurred in the Course of Quinidine Therapy*

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PERSISTENT ventricular fibrillation in man is incompatible with life. With its onset there is unconsciousness, and when it continues for more than a few minutes, death ensues. This occurs because the cardiac output falls to a level far below that necessary to maintain an adequate circulation. Clinically, then, ventricular fibrillation is manifested by syncope or sudden death. How frequently ventricular fibrillation is responsible for syncope is unknown. It is significant, however, that in the few instances in which electrocardiographic studies have been made during attacks of unconsciousness, flutter or fibrillation of the ventricles has been revealed in several. It is further significant that but few instances of heart-block and ventricular standstill are on record. This has been regarded as the common mechanism of syncope and sudden death in the Morgagni-Adams-Stokes syndrome. Lewis believes that ventricular fibrillation is probably the chief cause of fatal syncope.

This abnormal rhythm is, then, of importance to the clinician. His immediate problems are: (1) under what conditions does it occur; (2) what are its precursory mechanisms, and (3) how is it influenced by drugs. The purpose of the present communication is to discuss these problems and to report an additional case† of ventricular fibrillation or flutter-fibrillation proved by electrocardiogram.

The characteristic features of fibrillation of the ventricles in man were reviewed by Lewis in the third edition of his *Mechanism and Graphic Registration of the Heart Beat*. Since the publication of this edition several other likely cases have been reported by Reid,[2] Haines and Willius,[3] Levine and Mattin,[4] Donath and Kauf,[5] von Hoesslin,[6] Gallavardin and Berard,[7] and De Boer.[15] The case which we report showed electrocardiographic abnormalities consistent with those previously accepted as criteria for circus movements of greater or less regularity occurring in the ventricles and corresponding to curves recorded from experimental animals in whom ventricular fibrillation was seen.

*From the First Medical Service of the Boston City Hospital.
†The case here described was outlined by Sidel and Dorwart[1] in their article *Quinidin Sulphate in Auricular Fibrillation*, but the electrocardiographic aspects were not fully considered.

The unusual feature presented by this case was the occurrence of syncopal attacks associated with the ventricular acceleration. These attacks were repeated many times during the last eight hours of the patient's life, and the cardiac mechanism is explained by electrocardiographic tracings taken during the attacks and in the intervening periods of consciousness.

CASE REPORT

V. L., a single woman of forty-eight years, was admitted to the Boston City Hospital January 19, 1926, complaining of shortness of breath of six months' duration. In July, 1925, she was confined to bed with an attack of dyspnea and orthopnea. Recovery was followed by moderate dyspnea on exertion, and on three subsequent occasions she had attacks of progressively severe dyspnea, orthopnea, and palpitation. The last attack began the latter part of December, 1925, since which time she had been confined to bed.

At the age of eleven she had her first attack of rheumatic fever. All joints were swollen, painful, and very tender. Following this she had attacks of rheumatic fever about every three years up to 1921.

From June 2, 1924, to June 18, 1924, she was a patient at the Boston City Hospital, her chief complaint at the time being shortness of breath and sore throat of ten days' duration. Her condition was diagnosed acute bronchitis. It was noted that for three years preceding this illness she had slight dyspnea on exertion. Examination on this admission showed a regular cardiac action except for occasional extrasystoles. There was some enlargement of the heart to the left as determined clinically and by x-ray examination. No other essentials were noted.

When admitted January 19, 1926, the patient was found to be a well-developed and well-nourished, middle-aged woman in moderate respiratory distress. Breathing was rapid and labored, and orthopnea marked. There was cough at intervals of a few minutes. Except for slight redness of the right side of the faucial ring the examination of the head and neck was negative. The chest was barrel-shaped expansion on both sides being moderate and equal. The heart was definitely enlarged to the left, the apex impulse being in the anterior axillary line 13 cm. to the left of the midsternum. At the apex a thrill, probably diastolic in time, was felt. The apex rate was 140, absolutely irregular in force and rhythm. The first sound at the apex was loud and booming, the second sound weak. Loud to-and-fro murmurs were present, but timing was difficult because of the rapid rate. The radial pulse rate was 80, the pulse deficit 60. The lungs were resonant throughout, and the breath and voice sounds were normal. At both bases posteriorly, from the midscapula down, there were numerous coarse râles most marked on the left. The liver was palpable three fingerbreadths below the costal margin in the midclavicular line. Spleen and kidneys were not felt, and there was no evidence of fluid in the abdomen. Slight pitting edema was present over both legs. The radial arteries were soft.

Blood pressure: systolic 140 mm. mercury, diastolic 90 mm. White blood cell count 8,000. Urine: no albumin, no sugar, normal sediment, specific gravity of 1.016. Blood Wassermann reaction negative.

Absolute rest, repeated doses of ¼ grain of morphine, to be given subcutaneously, and large doses of the tincture of digitalis were ordered. The patient did not do well, and because of her frequent vomiting the nursing staff did not push the digitalis to the desired extent. On January 23, 1926, digitora pills, grains ii, three times a day were prescribed.

The apex beat on January 23 was recorded at 120-140, with a pulse deficit ranging from 25 to 40. There was slight general improvement, but the patient was still orthopneic, and there were many râles at both bases. The edema of the legs had disappeared. A poor prognosis was given.

The dose of digitora was changed to grains i, three times a day, on January 24, because of nausea and vomiting.

The electrocardiogram of January 26 demonstrated auricular fibrillation and frequent ectopic ventricular beats. The ventricular rate was 90-103.

Impovement was noted on January 28, while on digitora, grains i, three times a day, the apical rate being 90-100 with a pulse deficit of from 5 to 15. The patient looked better and was comfortable in bed. There was very little dyspnea, and no râles were heard at the bases.

On January 30 digitalis was discontinued and quinidine therapy instituted. After a total of 61 grains (4 gm.) in three days the quinidine was discontinued because of the marked nausea and gastric irritability it evoked. For several days following, nausea and vomiting persisted and little food was taken.

Digitora, grains ii, three times a day, was again ordered on February 5, and discontinued February 8. During this period no drop in pulse deficit was obtained, the drug being stopped because of nausea and vomiting. On the eighth she was allowed up in a chair for a half hour daily, not because of any improvement, but merely to secure a better state of mind.

On the ninth it was decided to give quinidine another trial, and accordingly a total of 123 grains (8.2 gm.) was given by the thirteenth. This therapy was interrupted after an initial dose of 3 grains because of nausea and vomiting. Nevertheless it was continued the following day, although nausea was still present. The patient was up in a chair for short periods. Orthopnea, dyspnea on exertion, and râles at both bases were present. She continued to do poorly and died February 13, after eight hours of recurrent syncopal attacks.

POST-MORTEM EXAMINATION

February 14, 1926. Twelve hours post-mortem. Body length 158 cm.

Peritoneal Cavity.—Numerous fibrous adhesions between gall bladder and omentum and pelvis, between large and small intestines, uterus, left ovary and tube; liver was 7 cm. below xiphoid and 2 cm. below costal margin. No excess of fluid.

Pleural Cavity.—No excess of fluid. A few firm fibrous adhesions in the upper right pleural cavity.

Pericardial Cavity.—Patches of firm, fibrous adhesions were found between visceral and parietal surfaces in the region of the left ventricle and both auricles and about the large vessels. Elsewhere the surfaces were smooth and shining. No excess of fluid.

Heart.—Weight 475 gm. The heart was large, firm, and with a much dilated left auricle. On section the myocardium showed no evidence of fibrosis. The inner surface of the left auricle was firm, smooth, and pinkish gray-white. The mitral valve was much thickened and contracted. There was a point on the margin of the valve that was bright red, irregular, and about 2 mm. in diameter. This did not arise above the surrounding surface. The chordae tendineae were shortened, thickened, and grayish white in appearance. Fibrous tissue had replaced some of the tissue of the papillary muscles, making them grayish red, firm, and short. The myocardium between the mitral and aortic valves was denser, firmer, and grayer than normal. Multiple section elsewhere revealed no gross fibrosis.

Measurements:	tricuspid valve	12.0 cm.	Circumference.
	pulmonary valve	8.2 cm.	
	mitral valve	8.5 cm.	
	aortic valve	6.5 cm.	
	left ventricle	1.3 cm.	Wall thickness.
	right ventricle	0.5 cm.	

Lungs.—The whole right lung was red, fairly firm, but crepitant throughout. The left lower lobe was firm, red, but crepitant. On section these portions were red, wet, and oozed considerable amounts of blood.

Spleen.—Weight 255 gm. It was large, soft and grayish purple. On section the organ was soft, very dark purplish red, and much pulp could be scraped away.

Liver.—Weight 1620 gm. It was regular, smooth, firm, and brownish red with markedly rounded edges. On section the organ was firm, purplish brown, and lobulations were visible. Gall bladder and bile ducts were negative.

Aorta.—A few irregular yellowish areas were found on the abdominal aorta. Otherwise it was negative.

Brain.—Weight 1315 gm. The surface was firm and pinkish gray. Multiple sections revealed no pathological changes.

Anatomical Diagnosis.—Chronic auricular endocarditis, chronic endocarditis of mitral valve with mitral stenosis, congestion and edema of lungs, acute splenic tumor, old pericarditis, congestion of liver and spleen, old pleuritis, old peritonitis, multiple leiomyoma of uterus, simple cysts of ovary, mucous polyp of cervix, arteriosclerosis.

DISCUSSION OF SYNCOPAL ATTACKS

On February 13, 1926, at 4 P.M., three hours after the last dose of 15 grains (1 gm.) of quinidine, the patient developed an unusual combination of symptoms which were repeated in cycles and which ended in death eight hours later.

The following note was made by the house officer: "About 4 P.M. I was called to see the patient and found her lying propped up in bed breathing stertorously. This breathing quieted down and finally stopped completely. She became yellow and cyanotic; the muscles of the left arm and both forearms twitched. The apex beat could not be detected, but after a minute the heart began to come back. During all this time the patient was unconscious, but now with the return of the heartbeat the patient began to regain consciousness. About fifteen minutes later she went through the following cycle: the heart rate at the apex becomes slower and slower and finally stops completely. With this the patient swoons, losing consciousness. She becomes pale and yellow, and then takes on a peculiar deathlike tint. The respiration becomes deeper, then stertorous, and finally stops. Ten or fifteen seconds later twitching of the muscles of the face and left arm occurs. Then after the heart has been stopped (apparently) for two minutes and ten seconds, it gradually begins to beat again. The patient's color begins to return. The apex beat, at first absolutely irregular for about

forty beats, becomes more rapid and coupled. In this coupled state it remains until a second attack. At moments the apex beat appears irregular, simulating fibrillation. Atropine, caffein, and adrenalin have been of no influence on these recurring attacks."

The patient's breathing just after the apparent loss of the apex beat was of the character of Cheyne-Stokes respiration. The breathing became deeper, and more and more stertorous, gradually reached a summit and gradually declined. The active period comprised on the average about 30 respirations. Each respiratory phase was relatively short

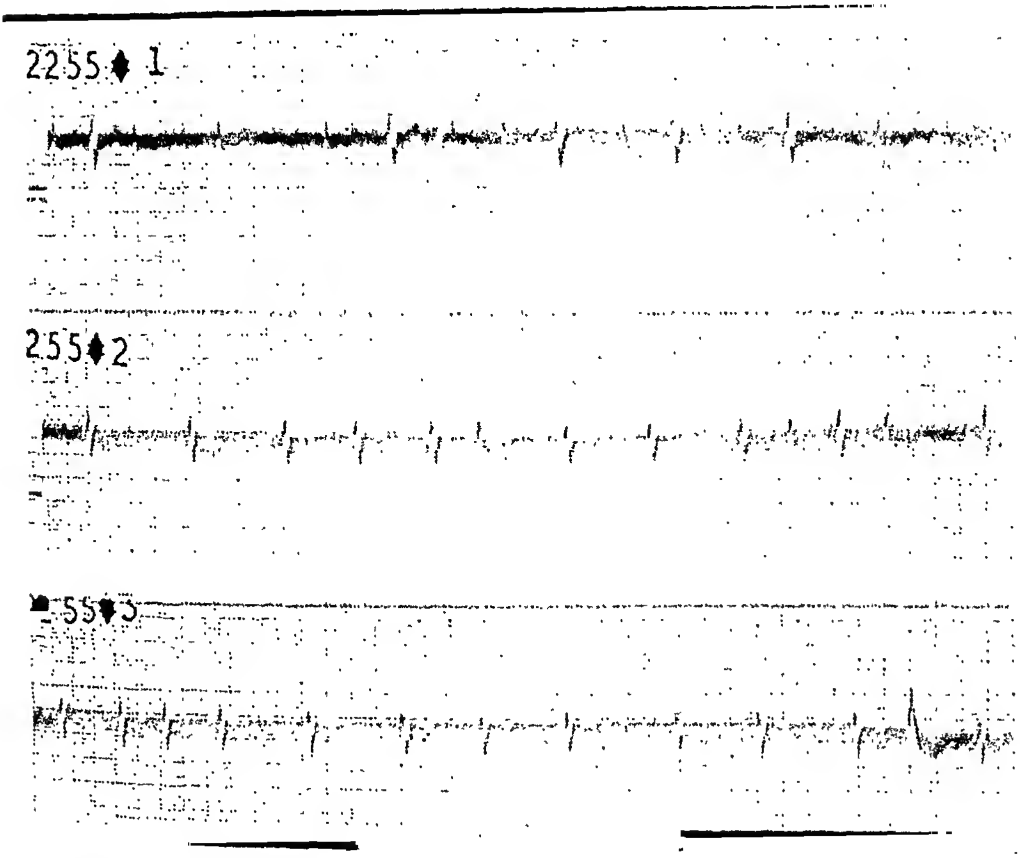

Fig. 1.—Electrocardiogram, Leads I, II, and III, January 26, 1926. Auricular fibrillation, ventricular rate 90-100, low voltage of ventricular complexes in all leads (amplitude not over 5 mm.), several ectopic ventricular contractions, especially in Lead I where alternate beats are abnormal for four couples following the fifth beat.

NOTE: In all figures scale on the ordinate in 10^{-4} volt, and on the abscissa is 0.04 second.

compared to the interval between. With the onset of the apneic period the patient was usually cyanotic and appeared dying. From ten to thirty seconds after this onset irregular beating at the apex could be detected and shortly after this the patient began to breathe slowly. Her color returned, and she gradually regained consciousness. With eyes wide open she gently moved her head on the pillow, slowly repeating that she could not live, that she was dying. These periods of consciousness lasted but a few minutes, and then the same cycle ap-

peared all over again. Thus for eight hours the patient vacillated from "death" to life about once every five or ten minutes.

When seen by one of us about three hours before death, the cyclic attacks were being frequently repeated. It appeard, however, that an

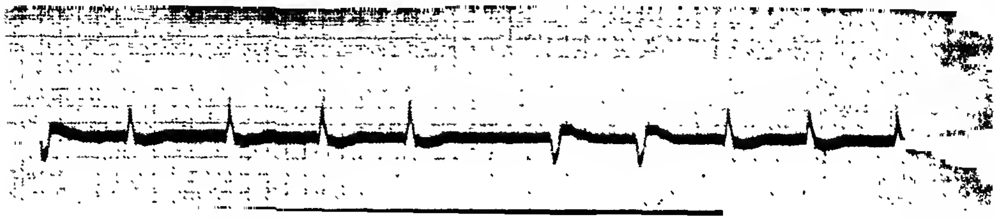

Fig. 2.—Electrocardiogram, February 13, 1926. Probable auricular fibrillation, ventricular rate 50-60, inverted T-waves, five complexes in opposite phase to the usual QRST deflections. NOTE: In this and the following illustrations the lead is either I or II, as a confusion arose in the original marking.

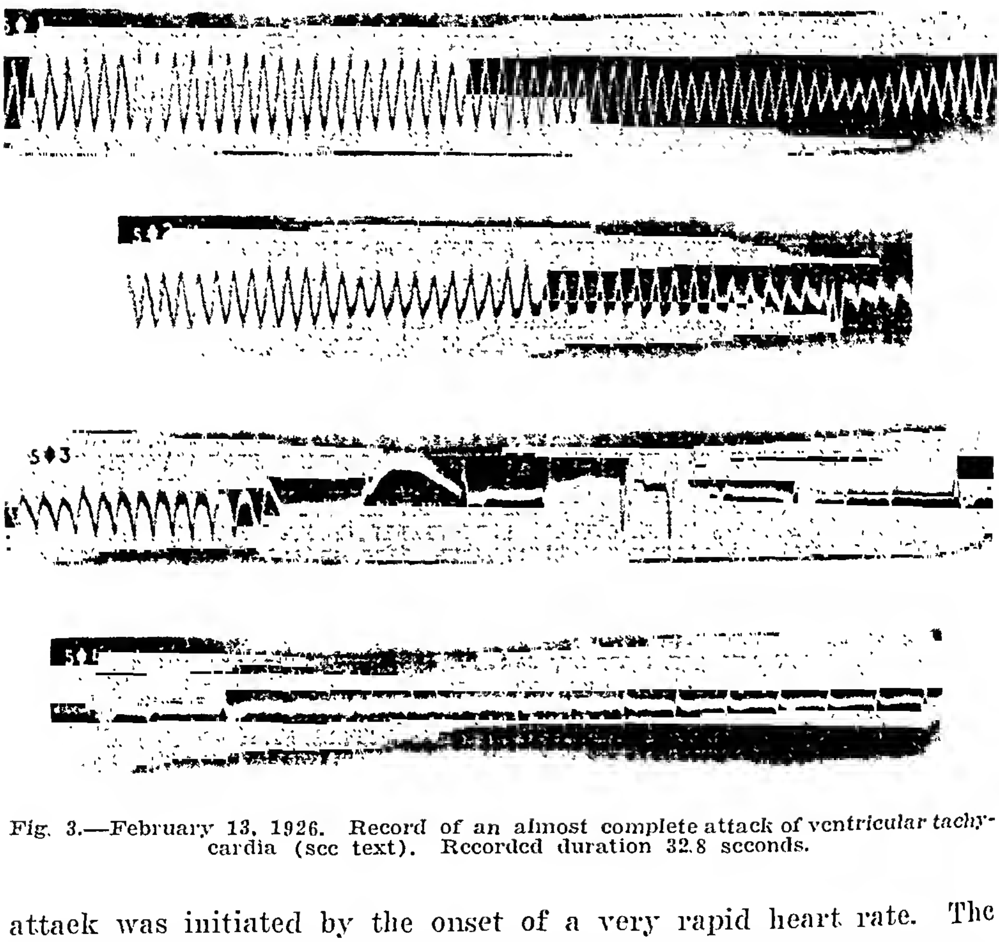

Fig. 3.—February 13, 1926. Record of an almost complete attack of ventricular tachycardia (see text). Recorded duration 32.8 seconds.

attack was initiated by the onset of a very rapid heart rate. The heartbeats were inaudible at the apex, but a trembling of the precordium could be felt during the time that this rate persisted, followed by the return of faint irregular beating of the heart at a much slower rate and finally the resumption of a relatively regular rhythm.

Electrocardiographic studies were made at this time. Technical difficulties and the long distance between the patient and the laboratory, with consequent telephone and hand signal relays, made accurate correlation between clinical and electrocardiographic records difficult. The electrocardiograms, however, are sufficiently clear to explain the mechanism of the attacks.

Fig. 1 is the electrocardiogram of January 26, 1926, eighteen days before the onset of the attacks preceding her death. It shows auricu-

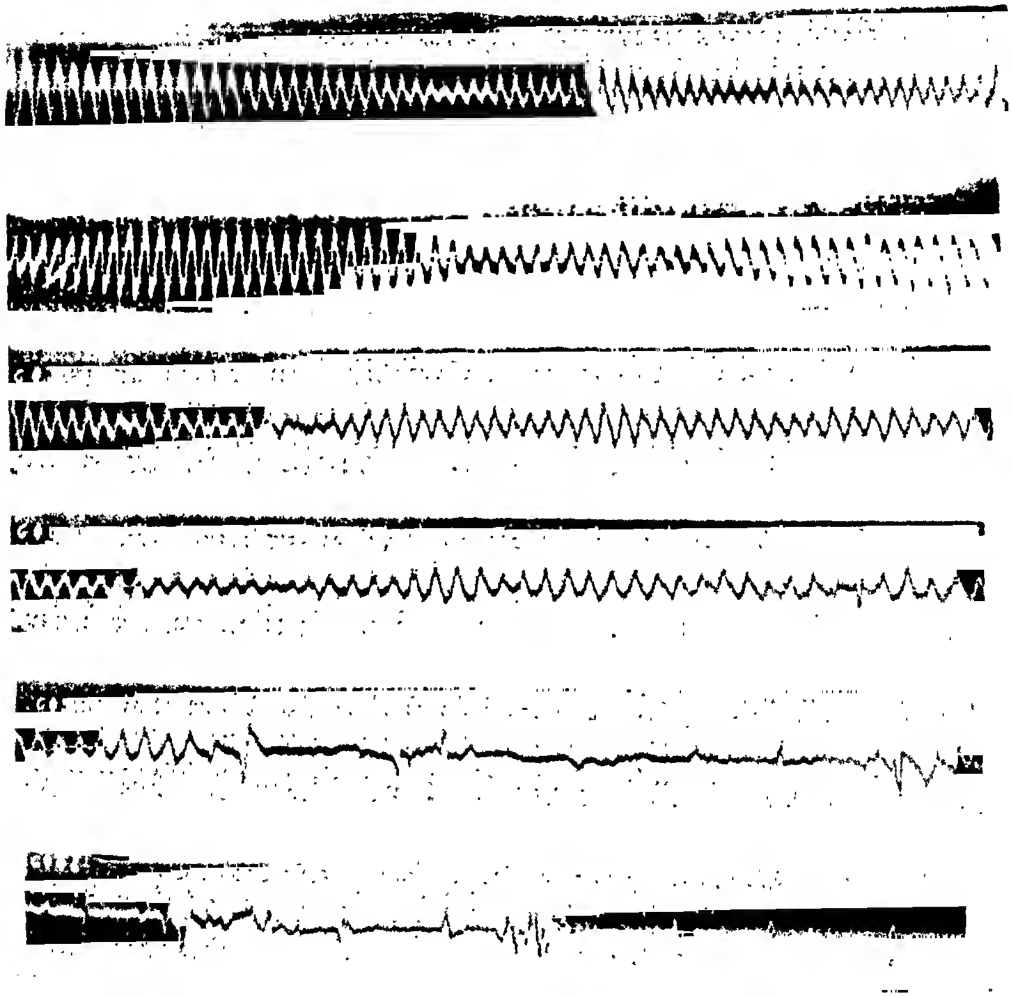

Fig. 4.—February 13, 1926. Record of another attack of tachycardia. Rate 220, slowing to 150 before the offset. Recorded length of paroxysm is about 71.6 seconds. Note temporary recovery of normal conduction in one beat near the end of strip 4.

lar fibrillation, rate 90-100, low T-waves in all leads, low voltage of QRS complexes (amplitude not over 5 mm. in any lead), and several ectopic ventricular contractions.

Fig. 2 is the record taken when the patient was seen by us February 13, 1926, and shows the type of rhythm existing between attacks of tachycardia. Absolute ventricular arrhythmia is present but with less evidence of auricular activity than in the previous tracing. The more

aberrant ventricular complexes are inverted and slurred. The rhythm resembles that seen in patients who are intoxicated by digitalis in whose electrocardiograms regular alternation in direction of the QRS complexes sometimes appears in attacks of tachycardia. The rate is 50-60. It is possible that auricular standstill is present.

Fig. 3 shows an almost complete attack of tachycardia, the tracing starting as soon after the onset as it was possible to start the electrocardiograph. During this attack the patient lapsed into unconsciousness as previously described. The first part of the record shows a regular diphasic oscillation of the string shadow at a rate of 230-250. There is a slow waxing and waning of the amplitude of the deflection. This phasic variation has been noted by Lewis[13] in experimental ventricular fibrillation. It is probably related to a change in electrical axis of the circulating wave in the ventricle as it alters its course. As the attack progressed the rate fell (in the second strip) to 210 and the complexes have more the form seen in paroxysmal ventricular tachycardia. The offset of the attack is abrupt after a recorded duration of 32.8 seconds. A short period of gross arrhythmia follows, succeeded by a regular rhythm at a rate of 80.

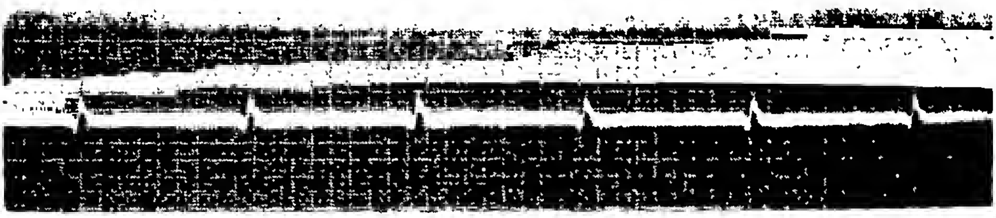

Fig. 5.—Record taken after patient had stopped breathing and was, to all appearances, dead. Rate 33 and regular. Probable auricular standstill.

A similar attack is shown in Fig. 4. The early part of this record shows a rate of 220, but this is reduced to 150 at the end of the paroxysm. Small waves present in the last strip suggest auricular activity, but many artefacts were caused by muscular movements of the patient.

Fig. 5 is an electrocardiogram taken after the patient had stopped breathing and was dead. It shows slow, regular, ventricular beats at a rate of 33 per minute. This cardiac action continued for several minutes after all other signs of life were absent.

DISCUSSION OF MECHANISM OF VENTRICULAR FIBRILLATION

The exact mechanisms acting in the human heart during ventricular fibrillation are as yet unknown. It seems clear, however, that the patient here reported was suffering from an abnormal rhythm best considered as fibrillation of the ventricles or perhaps more accurately as a preliminary rhythm to fibrillation, of the nature of ventricular

flutter. The predominating regularity of the oscillations at a rate not exceeding 250 is in favor of the latter diagnosis.

It is probable that the mechanism in ventricular fibrillation is similar to that known to occur in the auricles, and is produced by the development of a circus movement. The general character of the curves obtained is in favor of this hypothesis, and the forms of the different tracings recorded in the literature may represent stages analogous to those of fibrillation, flutter-fibrillation, and pure flutter of the auricles. The presence of highly specialized conducting tissues in the ventricles adds to the complexity of the circus movement when occurring in that chamber of the heart. An electrocardiogram published by Kerr and Bender[8] shows a very rapid and irregular oscillation of the string, at a rate of about 1000 per minute. This would more accurately correspond to what we call fibrillation in the auricles, in contrast to the slower and more regular rhythm recorded in our case.

QUINIDINE AND VENTRICULAR FIBRILLATION

Digitalis and quinidine have both been held responsible for ventricular fibrillation in man. Both drugs had been given in full doses to the patient we are reporting. In the case described by Kerr and Bender[8] attacks of syncope occurred in the course of quinidine therapy, and were shown by electrocardiograms to have been related to periods of rapid ventricular tachycardia, such as we are describing. An attack was initiated at one time in their case by the administration of 3.6 grams of quinidine sulphate in four days. In our patient 8.2 grams were given in four days.

The occurrence of unexplained death in the course of quinidine therapy has been the chief objection to its use. Because of this possibility this valuable drug has been discarded in many clinics. Attacks of syncope[8] have been noted in the course of quinidine therapy, and at least in two instances such syncope has proved to be associated with the onset of ventricular fibrillation. It has been shown[10] that the usual mechanism of quinidine death in cats is by respiratory paralysis. How often this mechanism has been responsible for death in man is unknown. More observations on the mode of death in higher mammals would throw light on this problem. As Garry[11] has shown, it is easier to produce ventricular fibrillation in the hearts of larger animals.

DE BOER'S THEORY OF QUINIDINE ACTION IN VENTRICULAR FIBRILLATION

The mode whereby fibrillation in the ventricles is produced is unknown. Lewis suggests that it may be the production of a circus movement through reëntrant ectopic beats. De Boer[12] has recently discussed the problem in an article entitled *Ventricular Fibrillation in Complete Heart-Block and the Action of Quinidine and Quinine Preparations in Heart-Block*. He emphasizes the fact that these preparations

alter the metabolic condition of the ventricular muscle so that variations in the refractory period occur irregularly in different parts of the heart, and permit of the development of a circulating wave from reëntrant ectopic beats. Moreover in auriculoventricular block the protecting influence of the His-Purkinje system is in abeyance. If intraventricular block is also present, the danger from quinidine in producing ectopic ventricular beats with circus movements is greatly increased.

De Boer appreciates what seems to us to be the important factor in the development of ventricular fibrillation, namely, the significance of the conducting system in preventing the development of circulating waves in ventricular muscle. His conclusions, however, are somewhat different from ours.

THEORETICAL FACTORS IN THE PRODUCTION OF VENTRICULAR FIBRILLATION

Let us first consider the physiological control normally operating to prevent an excitation, arising in the ventricular musculature, from going on to the production of circus movements in the ventricle. Extrasystoles are of common occurrence, but examples of reexcitation are infrequent.

Ventricular premature contractions are known to be followed by a compensatory pause which is due to a condition of refractoriness. This refractoriness is uniformly distributed over the entire musculature, and it is probable that such a generalized refractory state is responsible for the prevention of reexcitation and formation of circus movements. It is also probable that the uniform refractoriness of the ventricles as a whole is brought about by the elaborate conducting system in the ventricles: the bundle tissue, its branches, and the Purkinje fibers. An excitation that arises from a focus in muscle spreads in all directions and quickly reaches the endothelium and Purkinje fibers. Through these fibers it is quickly distributed to all parts of the ventricles. Conduction in ventricular muscle proceeds at a rate of about 450 mm. per second, whereas conduction in the Purkinje fibers varies from 2000 to 3000 mm. per second—from four to six times as rapidly. This permits an excitation spreading through the Purkinje fibers to intercept the excitation process spreading through muscle from the original focus, and in this way the entire muscle contracts almost simultaneously and is left in a generalized refractory state.

If it is allowed that the integrity of the bundle tissues and the Purkinje system normally prevents the formation of circus movement in the ventricles, then it would follow that depression, disease, or injury to these tissues would predispose or lead to fibrillation of the ventricles. This, we believe, is the chief factor. Both quinidine and digitalis are known to depress these tissues. However, in the cat quinidine usually kills by respiratory paralysis and digitalis by its

action on the ventricular muscle, before, according to the theory, the damage to the bundle tissue and Purkinje system, per se, is great enough to precipitate fibrillation.

Lewis[14] and his coworkers have studied the action of quinidine on the heart of the dog and demonstrated that quinidine greatly depresses the auriculoventricular node and bundle tissues of the dog's heart. A lengthening of the P-R intervals is regularly noted. A single dose of 0.1 gram given to dogs increased the QRS duration of the electrocardiogram by about 20 or 30 per cent. Repeated doses increased the time by 50 or 70 per cent. It is likely that quinidine in man has a similar depressing action on the bundle branch and Purkinje tissues.

In its action on the fibrillating auricles quinidine was found to (1) slow the rate of conduction, and (2) increase the refractory period. According to their experiments both actions were marked—an increase in the time of conduction and the lengthening of the refractory period amounting to about 100 per cent with large doses. The following factors will theoretically favor the continuation of circus movements in a muscle: (1) a long path or circuit, (2) a slow rate of conduction, (3) a short refractory period. In the fibrillating auricles the main path is usually confined to a ring about the great veins of the right auricle. In the ventricle, as far as is known, there is no one special circuit, and judging from the curves obtained, the circuit may be considerably longer than the path existing in auricular fibrillation. The rate of conduction in the ventricular muscle is approximately one-half the rate in the auricles (auricular rate 1000 mm. per second, ventricular rate 450 mm. per second). The longer circuit and the slower rate of conduction in the ventricular muscle favor circus movements by insuring a larger responsive gap. These conditions may be so favorable as to be but little influenced by quinidine. Further, the effects of its action on rate of conduction and the length of the refractory period tend to balance each other. This appears to explain why quinidine, a drug which abolishes fibrillation in the auricles, is unable to prevent the inception of fibrillation in the ventricles. On the contrary, by its depressing action on the bundle tissue and because of favorable conditions in the ventricles, fibrillation may be favored.

RELATION OF HEART-BLOCK TO VENTRICULAR FIBRILLATION

Five of 13 reported cases of ventricular fibrillation occurring in man were associated with complete heart-block as the underlying rhythm, either preceding or following the fibrillation. In the case reported here the rhythm, also, appeared to be governed from an infra-auricular center. All five cases with complete heart-block showed syncope or Adams-Stokes syndrome during the period of fibrillation. The question raised is how often is ventricular fibrillation the underlying mechanism in attacks of syncope known as Adams-Stokes syndrome. This

condition occurs in patients with disease of the bundle tissue and the usual supposition is complete ventricular standstill. As but few electrocardiographic studies have been made during such attacks, the frequency of ventricular fibrillation is unknown.

The poor prognosis in patients with disease of the bundle tissues suggests that coordinated ventricular action is dependent upon activity of the nodal centers situated in the bundle tissues. It would seem that with complete depression of these tissues ventricular action, save ventricular tachycardia or ventricular fibrillation, is impossible. This fact together with the noted association of heart-block and ventricular fibrillation is evidence in favor of the hypothesis presented above. From this theory it follows that a depressing drug acting on a bundle tissue already depressed by disease would find conditions favorable for the production of fibrillation. This seems to have been the situation in the case of Kerr and Bender and perhaps in the case we are reporting.

It is likely that depression of bundle tissues alone is the important precursor. The depression of the Purkinje system is of less importance for two reasons: (1) permanent ventricular rhythm governed by centers located below the bundles in Purkinje or muscle tissues is unknown, (2) depression sufficient to prevent simultaneous transmission from an active nodal center to all parts of the ventricle would have to be unusually extensive. The widespread Purkinje tissue is not as easily blocked as small centers confined to the bundle tissues.

THE MECHANISM OF CESSATION OF THE ATTACKS

The mechanism by which ventricular fibrillation is brought to a close remains to be discussed. We will recall that in our case the rhythm was governed from an infra-auricular center. An analysis of our tracings suggests that this center was not constant, but varied. It is apparent that the depression of the bundle tissues and Purkinje system that we hold responsible for the onset of fibrillation, recovered sufficiently to permit transmission. If this recovery took place in the presence of circus movements in the ventricular muscle, those circus movements would theoretically be brought to a close by the first excitation arising from the node and distributing through the Purkinje system to the musculature. This would destroy any responsive gap and result in a general state of refractoriness from which the ventricle would recover and permit the continuity of rhythmic control from the nodal center. As long as the nodal center and Purkinje fibers remained excitable, this rhythm would continue. With the reappearance of further depression, fibrillation might be precipitated again. The character of the tracings in the interfibrillation periods suggests incomplete recovery in the bundle-branch tissues.

De Boer believes that the intact conducting system prevents initiation of ventricular fibrillation in the normal heart by permitting the

diffusely distributed impulses of contraction to neutralize each other in all parts of the heart at one time. We would suggest that the development of a generalized refractory state of ventricular muscle following contraction brought about by a normal Purkinje and His system conduction is responsible for the prevention of reëntrant beats and circus movements. De Boer also believes that the cessation of an attack due to quinidine can be explained by a further action of the drug in so altering the refractory period that the circulating wave meets a wall of refractory muscle. A similar effect could occur with recovery and activity of the auriculoventricular node and conduction system. Impulses from node to Purkinje fibers would theoretically produce a totally refractory ventricular muscle, and thus *end* the circus movements. It is probable that quinidine has important actions on both ventricular muscle and conduction systems. It is our impression that influences on the latter are of major significance.

DIGITALIS AND VENTRICULAR FIBRILLATION

A corollary from this analysis would concern the part played by digitalis in the pathogenesis of ventricular fibrillation. It would appear likely that there is danger of precipitating such an abnormal rhythm by digitalis, in cases in which there is disease of the His bundle and its branches, by its depressing effect upon these tissues. Depression of the idioventricular center, especially if the branches of the bundle show evidence of lowered conductivity, would certainly favor such a rhythm. Moreover, this consideration would make it appear safer to omit digitalis during quinidine therapy, since the danger of inducing ventricular circus movements is minimized by the presence of an intact conducting system.

SUMMARY

1. A patient with rheumatic heart disease with syncopal attacks and death is reported with clinical, electrocardiographic and autopsy findings.

2. Electrocardiographic study showed the mechanism in the heart, during unconsciousness, to be a probable circus movement in the ventricles, of the nature of flutter or fibrillation, associated with auriculoventricular dissociation and auricular fibrillation or standstill.

3. The patient had received both digitalis and quinidine sulphate in moderately large doses. The possible influence of these drugs in initiating ventricular fibrillation by depression of the His-Purkinje system is discussed.

4. Patients with combined auriculoventricular and intraventricular block are particularly liable to ventricular circus rhythm if the conducting tissues are further depressed by digitalis or quinidine.

5. On theoretical grounds the use of quinidine to restore normal rhythm in auricular fibrillation would seem to be safer when it is not administered in combination with, or directly following digitalis. This conclusion is more definite when intraventricular block is present.

We wish to express our thanks to Dr. Ralph C. Larrabee for his permission to study and report this case.

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THE DEVELOPMENT OF THE ABNORMAL COMPLEXES OF THE ELECTROCARDIOGRAM IN CORONARY OCCLUSION*

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At the present time most clinicians believe that occlusion of a coronary artery is usually accompanied by a definite clinical syndrome. Herrick[1] in 1912 first accurately described in the American literature, the clinical signs and symptoms of this condition, which until that time had been confused with angina pectoris. The excellent papers of Longcope,[2] Wearn,[3] Hamman,[4] and many others in the last decade have led to a better definition of the signs and symptoms which follow sudden occlusion of a coronary artery with resulting infarction of cardiac muscle.

While contributions were being made to the recognition of the clinical syndrome accompanying this condition, investigators were studying, by means of electrocardiograms, deviations of the electrical currents which occur when cardiac muscle is injured by artificial means. Having this experimental basis, clinicians began to observe the changes in the electrocardiogram which take place when patients suffered from occlusion of a coronary artery.

In 1909 Eppinger and Rothberger[5] observed very unusual alterations in the electrocardiogram when an area of the left ventricular muscle of a dog was destroyed by the injection of silver nitrate into the cardiac wall. This change was characterized by marked alterations in the QRS complex, the R-T segment arising high on the descending limb of the R-wave. Gradual lowering of this segment followed until it became isoelectric. The final summit of the R-T segment was designated the T-wave by these authors.

Later, Samojloff[6] observed similar changes in the form of the electrocardiogram in experiments carried out on the hearts of frogs. When an area of muscle near the apex was traumatized, elevation of the R-T segment above the base line occurred. Such changes were of short duration, returning to normal on the death of the injured area of muscle.

In 1918, Smith[7] ligated branches of the coronary arteries of dogs; he observed similar rises in the R-T segment above the isoelectric level in a large percentage of his animals. He likewise designated the final summit of the R-T segment the T-wave and noted that in time it gradually approached the base line and finally became negative.

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In 1920, Smith[8] found that interruption of the blood supply to the apical region of the left ventricle gave the greatest exaggeration of this peculiar alteration of the electrocardiogram. He found also that ligation of the vessels supplying the right ventricle was not accompanied by these changes. Stewart[9] is of the opinion that at the present time a correlation cannot be demonstrated to exist between electrocardiographic signs and the specific coronary artery occluded. He arrived at this conclusion from a study of published records of patients dying of coronary occlusion in which the specific vessel involved was stated in the autopsy report together with the electrocardiographic changes which were observed. Otto,[10] however, has recently demonstrated that transient occlusion of a coronary vessel in dogs gives rather constant specific changes in the form of the electrocardiogram. It remains to be proved that such temporary occlusions have the same effect on the electrocardiogram as have the more permanent occlusions which occur in patients in the clinic.

Pardee[11] in 1920 obtained from a patient exhibiting the signs and symptoms which accompany occlusion of a coronary artery electrocardiograms which were somewhat similar to those which Eppinger and Rothberger[5] and Smith[7] had previously described. By inference Pardee concluded that the presence of distortion of the R-T segment was a sign of occlusion of a coronary artery. He further observed in this case that shortly after the alteration of the R-T segment the T-waves became inverted in all three leads. He also directed attention to the large amplitude and sharp spiking of the T-waves. Since the patient recovered and lived for two years, certainty of the pathological lesion which was present at the time of the attack is lacking.

In 1922 Kahn[12] intimated that increase in amplitude of the T-wave of the electrocardiogram, followed later by sharp inversion and gradual return to the isoelectric level, was a characteristic sign of coronary occlusion. His records also revealed the R-T segment in Lead I arising from the descending limb of the R-wave, slightly above the base line. At autopsy it was demonstrated that coronary thrombosis was the pathological lesion.

Wearn[3] in 1923 described certain alterations in the T-waves of the electrocardiograms derived from ten patients suffering from coronary occlusion. Because of the variety of changes which were observed he was of the opinion that no one form of the electrocardiogram was characteristic of this condition. The necropsy reports were combined in such a manner that individual pathological lesions could not be associated with corresponding change in the T-waves.

In 1923 Smith,[13] in reporting studies of eleven cases of coronary occlusion, included the report of a patient in whom the descending

branch of the left coronary artery had been ligated. The electrocardiogram obtained from this patient nineteen days after operation revealed negative T-waves in all three leads. They remained negative for a period of eight and one-half months; at the end of this time they were found to be positive in Leads I and II. Smith concluded from his observations on this series that decreased amplitude of the QRS complexes as well as changes in the T-waves were of diagnostic value.

Oppenheimer and Rothschild[14] in 1924, in a report of a series of cases of coronary occlusion that came to autopsy, placed emphasis on distortion of the R-T segment and the characteristic rise of this segment from isoelectric level. They noted that the distance between the R-T segment and the base line must be 0.1 millivolt to be of significance. They designated the second summit of the R-T segment the T-wave and observed that the T-wave became more separated from the R-wave by an upward convexity as the segment approached the isoelectric level. They called this convexity the "cove plane" T-wave. Pardee[15] in his series designated as "coronary T-waves" waves which were similar in form to those just described.

Willius and Barnes[16] in 1925 reported changes in the T-wave in eight cases of coronary occlusion. The most frequent change observed was negativity of the T-wave in Lead I; less frequently there was irregularity of this wave in one or both of the other two leads. Two patients in whom the electrocardiograms showed elevation of the R-T segments came to autopsy; occlusion of the coronary artery was the pathological lesion.

Recently, Parkinson and Bedford[17] published a series of twenty-eight cases in which they were of the opinion that the lesion was cardiac infarction following coronary occlusion. Six of the patients died; four of these came to autopsy; in these the clinical diagnosis was found to be correct. That is to say, cardiac infarction was the pathological lesion. As the most usual electrocardiographic phenomenon they observed deviation of the R-T and S-T segments of the ventricular complexes from the isoelectric line. The deviation usually measured 1.3 mm. but sometimes reached 6 mm. (10 mm. equal 1 millivolt). In the majority of their cases they found the R-T or the S-T deviation was best seen in Leads I and III. The deviations were always opposite in direction in these two leads. Elevation in Lead I was found to be as frequent in occurrence as depression.

In the experimental and clinical studies just reviewed, reference has been made to several authors who have designated as a T-wave the final summit of the R-T segment of their records. Parkinson and Bedford are of the opinion, however, that this portion of the R-T segment should not be so designated. They publish records in which definite T-waves appear before the R-T segment returns to the iso-

electric level. These T-waves are always opposite in direction to the initial deviation of the R-T segment.

Parkinson and Bedford from an analysis of the records of their own patients, as well as of those of others, express the opinion that the form which electrocardiograms assume following coronary occlusion falls into one of two main groups: in one group the T-wave is negative in Lead I and sharply positive in Lead III; in the other group the T-wave is positive in Lead I and negative in Lead III. They designate these groups the T 1 and T 3 types respectively.

There seems therefore to be evidence, experimental as well as clinical, that sudden closure of a branch of a coronary artery is usually accompanied by a change in the ventricular complex of the electrocardiogram. On searching the literature there is a surprising scarcity of complete series of electrocardiograms illustrating the types of changes that may occur in this condition and the transformation and development from day to day of various abnormal complexes that follow infarction of cardiac muscle.

It is our purpose to report the clinical course of a patient exhibiting the signs and symptoms of coronary occlusion, together with a series of electrocardiograms illustrating the progressive development of changes in the QRS and T-waves. These curves resemble closely the development of the T-wave schematically proposed by Parkinson and Bedford. We have failed to find in the literature a similar series of electrocardiograms which show the successive steps in the evolution of the abnormal waves which are said to be characteristic of this lesion.

CASE HISTORY

C. B., was a white man, single, 38 years old. He worked as a chauffeur. He was admitted to the hospital on Nov. 25, 1927, at 10 P.M., complaining of severe, stabbing precordial pain of two hours' duration. He was discharged from hospital on Jan. 13, 1928.

Present Illness.—The patient's illness began thirty-three hours before admission. While laying a carpet in his home he felt a sudden twinge of mild but sharp substernal pain. The pain did not radiate nor was it severe enough to cause him to stop work. It lasted about five minutes. Four hours later he experienced a similar attack while cranking an automobile. This attack was more severe than the first but was approximately of the same duration. He drove his car the remainder of the evening without difficulty. The next day he was free of symptoms. He was aware of nothing unusual except for slight loss of appetite. The following evening (two hours before admission to hospital) he was seized with very severe, stabbing substernal pain which did not radiate. He described it as "something squeezing his heart." He became dyspneic and went into a state of collapse. Pain persisted for one-half hour. He was given morphia 32 mg. in divided doses. Partial relief followed. Pain persisted while he was being moved to hospital; dyspnea likewise persisted but was not marked. He was nauseated.

Past History.—The patient had been well until the onset of the present illness. He did not recall being confined to bed before this. He had usually been active, but he had never worked at hard labor. He had experienced frequent mild attacks

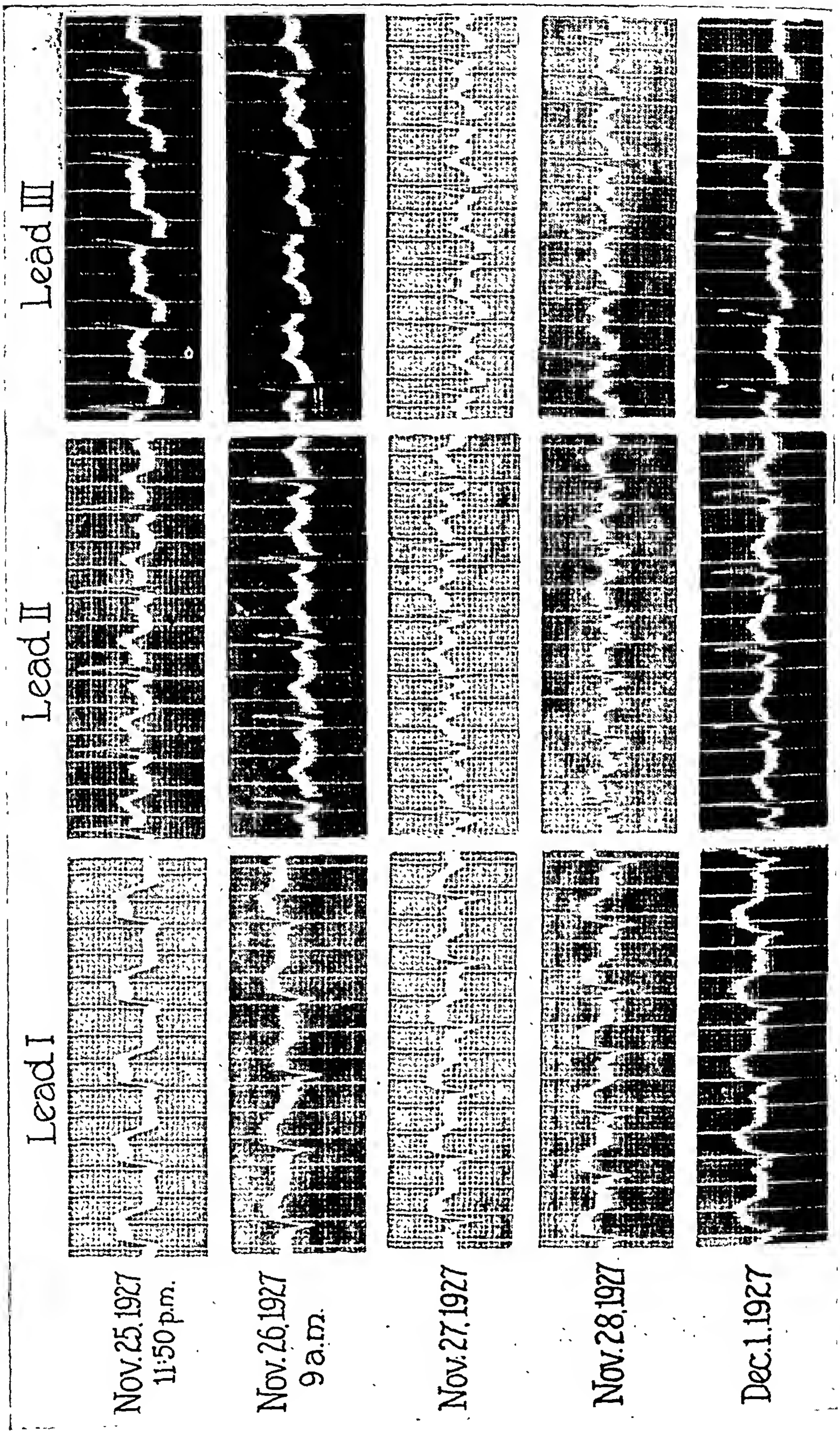
of headache for a number of years. He had been conscious of dyspnea on exertion during the past year. This symptom, however, had not interfered with his occupation. He had never experienced precordial pain nor palpitation. He had never been aware of the presence of edema. There was no history of gastro-intestinal disorders. The patient had gonorrhea at 22 years of age. There had been no recurrences. He had a chancre at 23 years of age, following which he was given several courses of salvarsan. No secondary symptoms of syphilis developed. Of two Wassermann tests made of the blood at the end of the antiluetic treatment, one had been negative and the other 4 plus. He used tobacco in moderation. He did not use alcohol.

Physical Examination.—The patient was an unusually large and well-developed white man. He appeared from ten to fifteen years older than his stated age. The skin was cold, moist and ashen gray. He was slightly dyspneic. The temperature was 100° F. (rectal), the pulse rate 90 per minute and the respirations 26 per minute. Eyes: There was slight bilateral arcus senilis. The pupils were equal and regular. They reacted promptly to light and in accommodation. The ears, nose and mouth appeared normal. There were no abnormal pulsations in the neck. The lungs were resonant throughout. There were a few fine moist râles at both lung bases posteriorly. Heart: There was no precordial thrill. The point of maximal impulse could neither be seen nor felt. The rhythm of the heart was regular; the rate was 90 per minute. The cardiac sounds were faint. There were no murmurs heard over the precordium. A friction rub was not present. The peripheral vessels were slightly thickened. The radial pulse was regular but weak. The systolic blood pressure measured 140 mm. of mercury, the diastolic 90 mm. The examination of the abdomen was negative. Extremities: There were no deformities. There was no edema of the feet. Glandular System: There was no generalized enlargement of the lymph nodes. Nervous System: The superficial and deep reflexes were present and normal.

Laboratory Examinations.—On admission to hospital, the urine showed a faint trace of albumin; the sediment was normal. The count of the white blood cells was 29,000, 92 per cent of which were polymorphonuclear in form and 8 per cent mononuclear. The count of the red blood cells was 4,800,000. The hemoglobin was 90 per cent (Dare). Fluoroscopic examination one hour after admission revealed that the lungs were clear and the hilus shadows were normal. The movements of the diaphragm were slightly limited on both sides. The heart did not appear enlarged. It occupied a transverse position. The aortic shadow was slightly widened. The Wassermann reaction of the blood at the end of the febrile period was negative.

Course in Hospital.—Immediately following fluoroscopic examination there was marked recurrence of pain. The radial pulse became weaker. The administration of morphia 16 mg. and nitroglycerine 0.64 mg. afforded considerable relief. The pain over the precordium continued throughout the night; it was, however, dull and less severe than during the evening. Pain continued for the next three days. The temperature ranged from 102° to 103° (rectal) during the first week, fell to 100° during the second, and then became normal. The pulse rate at first varied between 120 and 140 per minute and then fell to 100 per minute. The systolic blood pressure fell to 105 mm. and the diastolic to 80 mm., from having been at a systolic level of 140 mm. Certain changes occurred from day to day in the electrocardiograms (see description of electrocardiograms). The patient remained in bed for six weeks, began sitting up and walking during the seventh, and then went to the country for convalescence. He was free of symptoms on discharge from the hospital.

The patient returned to hospital twelve months later for examination. He had continued to work as a chauffeur. Dyspnea on exertion was still present; it


Lead I
Lead II
Lead III
Nov. 25, 1927 11:50 p.m.
Nov. 26, 1927 9 a.m.
Nov. 27, 1927
Nov. 28, 1927
Dec. 1, 1927

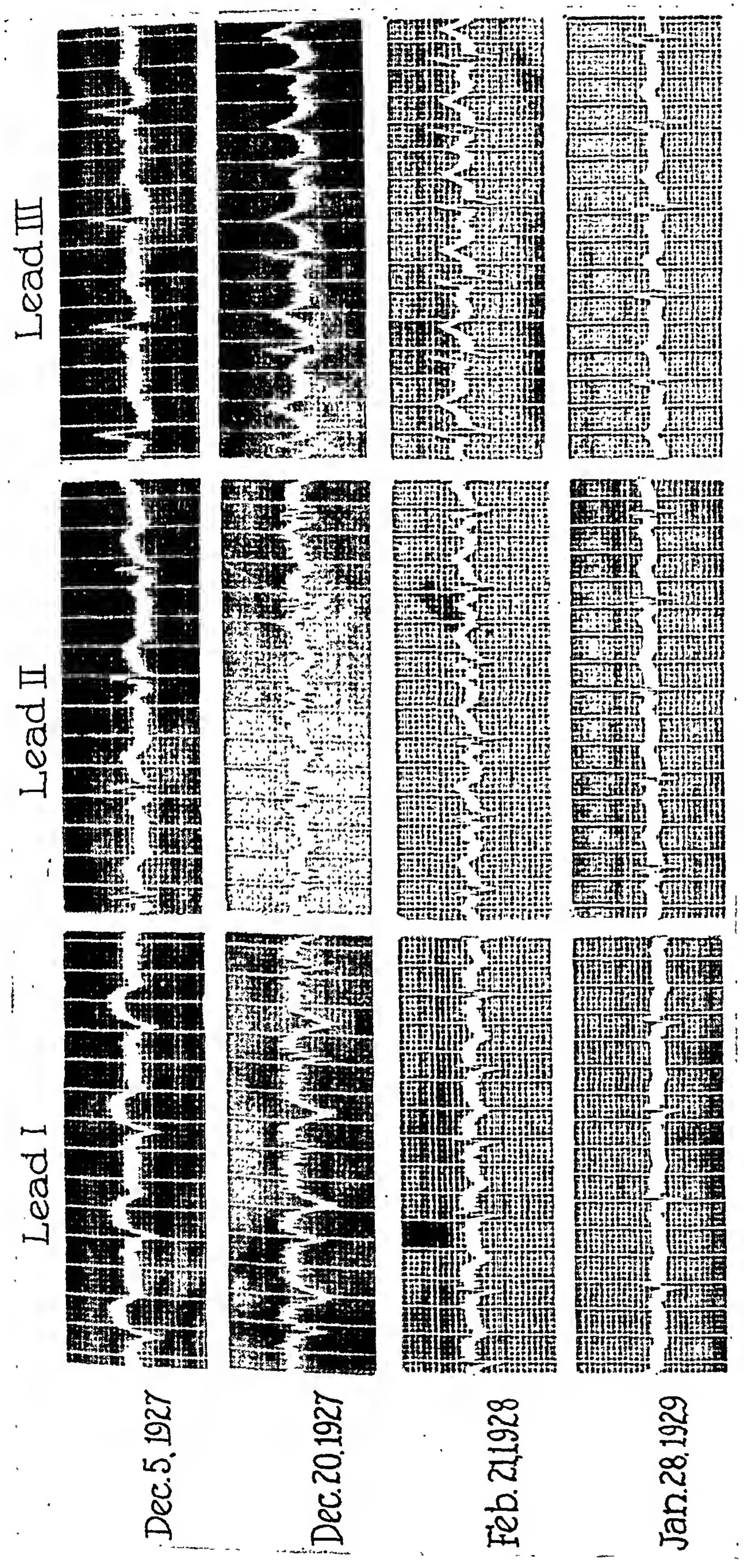


Fig. 1.—In this figure are reproduced electrocardiograms derived from a patient following an attack of coronary occlusion. The series illustrates the successive changes in the R-T and S-T segments and the evolution of the T-waves. For description see text. In these records the ordinates are 0.04 of a second apart; the abscissae 10^{-4} volts. The standardization in all records was such that 1 cm. equals 1 millivolt.

had not, however, increased in severity. He had experienced no cardiac pain. Examination of the heart was essentially the same as on discharge from the hospital except that over the pulmonic area there was distant slurring of the second sound extending into early diastole. The systolic blood pressure measured 122 mm. of mercury and the diastolic 78 mm.

The diagnosis* of this patient was.—Etiological: syphilis (?); anatomical: coronary occlusion; physiological: sinus rhythm.

Electrocardiograms.—The first electrocardiogram, taken four hours after the onset of the attack shows the R-T segment in Lead I originating directly from the peak of the R-wave (Fig. 1). There is a secondary rise in the segment which in records similar to this one has been designated a T-wave by some authors. Lead III in the same electrocardiogram shows a depression of the S-T segment and the beginning of the positive T-wave. Slight R-T elevation is seen in Lead II. Ten hours later (Nov. 26, 1927, 9 A.M.), the electrocardiogram is somewhat altered. In Lead I the R-T segment is of less amplitude; it is preceded by a well-defined Q-wave. There is no secondary rise which suggests a T-wave. Lead III shows an S-T depression with a well-defined positive T-wave. An S-wave is present in Lead II. There is little change in the electrocardiograms taken on Nov. 27, 28, and on Dec. 1. Ten days after the attack (Dec. 5, 1927) there is in Lead I a slight negativity at the end of the R-T segment, in that the R-T segment approaches the base line, crosses the isoelectric level for a short distance and gives an indentation below the line. This minute negative wave is the precursor of the negative T-wave. Lead III of this record shows slight notching of the QRS complex. The QRS interval, however, is only 0.06 of a second. On Dec. 20, twenty-five days after the first electrocardiogram, the T-wave in Lead I is sharply inverted and is preceded by the convex R-T interval. Oppenheimer and Rothschild[14] and Pardee[15] are of the opinion that this sign is characteristic of coronary occlusion. The only instance of T-wave negativity in Lead II is seen in this record.

The electrocardiogram, taken two months later (Feb. 21, 1928) reveals a negative T-wave of less voltage preceded by the "cove plane" in Lead I and a positive T-wave of less amplitude in Lead III. Notching of the R-wave is still present.

Fourteen months after the attack (Jan. 28, 1929) the electrocardiogram shows low voltage of all the complexes. The T-wave is slightly negative and traces of the former "cove plane" are still present. In Lead III there is notching of the R-wave and positive T-wave of low amplitude.

The P-R interval in all of the electrocardiograms of the series in 0.12 of a second in Lead I and 0.16 of a second in Leads II and III.

DISCUSSION

Clinical observers agree that pain, shock and dyspnea are the three characteristic symptoms of coronary occlusion. The pain is usually severe but varies in intensity with the size of the artery occluded. It is usually precordial in location, but it may radiate to the abdomen, in which case it may simulate an acute abdominal condition. It may be present for only a few hours or it may last for days. Shock is usually observed. Its severity varies with the size of the vessel which is occluded. Accompanying shock is an ashen gray appearance of the skin. A fall in blood pressure usually occurs a few hours after the onset; it may, however, occur earlier and remain low for several

*This diagnosis conforms to the nomenclature of cardiac diagnosis approved by the American Heart Association, AM HEART J. 2:202, 1926.

days. Dyspnea is usually present. It may be only transient and of slight intensity or may be so severe that the patient gasps for breath. During the second twenty-four hours, fever and leucocytosis are always present. The fever varies from 100° to 102°, the count of the white blood cells from 12,000 to 20,000. Leucocytosis may persist from one to three weeks. Hamman[4] in reviewing the literature of the subject calls attention to other signs and symptoms which are present less constantly; to be mentioned are pericardial friction rub, suppression of urine, pulmonary edema, enlargement of the liver, albuminuria, and nervous symptoms.

The patient now being reported upon exhibited at the onset the cardinal symptoms of coronary occlusion, that is to say, pain, shock, and dyspnea. Shock, however, was not pronounced until twenty-four hours after admission. With persistence of pain, accompanied by a rise in temperature, leucocytosis and fall of blood pressure, the diagnosis of coronary occlusion appeared certain.

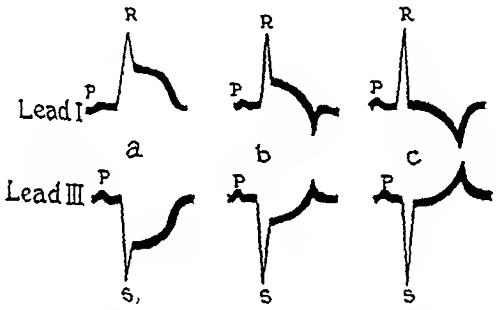


Fig. 2.—This figure is reproduced after Parkinson and Bedford. "Scheme illustrating the evolution of the plateau type of curve in Leads I and III. (*a*) Monophasic curve, reciprocal RS-T deviation in Leads I and III. (*b*) Intermediate phase, T-waves becoming evident. (*c*) Diphasic curve, T, of opposite sign in Leads I and III."

In the series of electrocardiograms of the patient taken on successive days can be traced the evolution of the plateau type of curve in Leads I and III such as was proposed by Parkinson and Bedford.[17] These authors devised a scheme which illustrates the successive stages. They were of the opinion that the ventricular complex is developed in three stages: the *monophasic* curve, the *intermediate* phase, and the *diphasic* curve (Fig. 2).*

The monophasic curve is seen in the electrocardiogram taken two hours after the occurrence of the coronary occlusion (Nov. 25, 1927). In Leads I and III there is reciprocal R-T and S-T deviation. The series falls therefore into the T-1 group. The first record indicates that the T-waves will eventually be negative in Lead I and positive in Lead III. The electrocardiograms taken on November 26, 27, and 28 further illustrate the monophasic stage, although a well defined Q-wave in Lead I and an upright T-wave in Lead III developed simultaneously ten hours after the first record. Three days later the R-T segment in

*We wish to thank Doctor Parkinson and Doctor Bedford for their kindness in giving us permission to reproduce this figure.

Lead I is convex; this is without doubt the precursor of the "cove plane" T-wave which is seen in the same lead in subsequent records.

The intermediate phase of the series is illustrated in the record taken on Dec. 5, 1927. The early negative T-wave is seen in Lead I as a negative depression of low amplitude after the R-T segment crosses the isoelectric level. The intermediate upright T-wave in Lead III developed before the corresponding wave in Lead I.

The diphasic curve illustrating the third stage in Parkinson and Bedford's scheme appeared in the electrocardiogram taken on Dec. 20, 1927. The sharply pointed negative T-waves of the "cove plane" type in Lead I and the similar but upright T-waves in Lead III are recognized as those often reported as being associated with coronary occlusion.

The changes which are seen to have occurred in the electrocardiogram three months after the occlusion (Feb. 21, 1928) are significant. If this record were examined alone, one would not suspect that marked alterations had occurred earlier in the R-, S-, and T-waves. That the curve is still of the diphasic type is of interest.

Fourteen months after the first record was taken (Jan. 28, 1929) all the complexes of the electrocardiogram are of low voltage. The only remnant which is left of the damage rendered by occlusion of a coronary artery is the slightly "cove plane" negative T-wave in Lead I.

Varying opinions have appeared in the literature as to the form which alterations of electrocardiograms of patients who have suffered from occlusion of a coronary artery assume. Wearn[3] expressed the view that there was no form typical of this condition. Another investigator[12] was of the opinion that most of the changes occurred in the T-waves. Abnormalities of the entire ventricular complex are, however, illustrated in the records of cases which have been reported.[11, 14, 15, 16, 17] Perhaps the confusion regarding the type of record associated with coronary occlusion is due in part to the varying lapses of time between the occurrence of the occlusion and the taking of the electrocardiogram. If this is correct, it is important that a larger number of complete series of electrocardiograms taken from patients who have suffered from occlusion of a coronary artery be published. It may be possible after a sufficiently large number of such series have been recorded to reconstruct the alterations in the electrocardiogram which have gone before and from a single record derive evidence that occlusion of a coronary artery had occurred at some earlier time.

SUMMARY

A report has been made of the case of a patient who exhibited the signs and symptoms which accompany occlusion of a coronary artery. Certain changes also occurred in the electrocardiograms. If these curves are arranged in serial fashion, the alterations which are ob-

served illustrate the evolution of the "coronary T-wave" in the manner that Parkinson and Bedford proposed in their scheme; that is to say, the monophasic, intermediate and diphasic stages which they described can be detected. No other series of records was discovered in the literature of this subject which illustrates these stages so exactly.

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THE OCCURRENCE OF THE CORONARY T-WAVE IN RHEUMATIC PERICARDITIS*

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SEVERAL observers have noticed that changes occur in the T-wave of patients who are suspected of having arteriosclerotic narrowing of the branches of the coronary system. One type of change has been observed immediately after thrombosis of a coronary branch and has been associated with cardiac infarction, while another type of change has been found to appear later after the infarction has had an opportunity to heal.[1] This latter T-wave abnormality has also been found in records of patients who have never had one of the severe attacks due to coronary thrombosis, but who have had the angina of effort which is associated with narrowed coronary branches.[2] This abnormality of the T-wave is seen in Fig. 1 and is characterized by a downwardly directed T-wave with the R-T or S-T interval showing an upward convexity, which lies either at the zero level of the record or above it. Changes in the T-wave or in the R-T or S-T interval have been reported by several observers as occurring in the course of acute rheumatic fever[3] and have been considered as evidence of myocardial damage caused by the rheumatic infection. In the course of study of a series of rheumatic patients in the wards of the city hospital, three patients have been observed whose electrocardiograms showed an abnormaliy of the T-wave which is practically identical with that described above as resulting from coronary narrowing, or following an infarction. These cases were all associated with a rheumatic pericarditis, and one of them came to autopsy.

CASE REPORTS

CASE 1.—A man, 48 years old, gave a somewhat doubtful history of rheumatism during his youth and had not had tonsillitis or sore throat to any extent. Before admission he had been ill in bed for one week, with what he called a cold. He was admitted complaining of marked shortness of breath with orthopnea and marked weakness. His temperature was 102° F., and his pulse was weak. His systolic blood pressure was 100 mm. and his diastolic 70 mm. The examination of the chest showed many rhonchi throughout. The heart sounds were distant and weak. There were no murmurs or pericardial friction rub. The liver was palpable four fingerbreadths below the costal margin. The Wassermann was negative. The x-ray examination showed considerable cardiac enlargement. The patient lived for three days, his temperature ranging from 100° to 103° F., and then he died.

The electrocardiogram taken the day before death is seen in Fig. 2. There is nothing noteworthy about the P-waves or the QRS group of this record except

*From the Medical Services and Cardiographic Department of the New York City Hospital.

the low voltage shown by the latter. The T-wave is turned downward in Lead I, and in the R-T interval there is seen an upward convexity which is much like that associated with localized coronary narrowing.

An autopsy was performed upon this patient, and the report from the pathological department by Doctor J. R. Lisa reads as follows: "The pericardium contains an excess of hemorrhagic fluid. The heart weighs 500 grams. The myocardiogram is hypertrophied and shows slight interstitial changes. The endocardium is smooth and shiny, and presents no abnormal features except for the valves. The mitral valve shows small, red, adherent vegetations about the size of a pinhead. The aortic valve is smooth and elastic and contains some sclerotic changes. The tricuspid valve is normal. The pulmonary valve is markedly sclerosed. The coronary vessels are patent and slightly thickened.

"*Microscopic:* The heart muscle of the left ventricle shows moderate hypertrophy. The mitral valve is thickened and fibrous. Beneath the epicardium is an

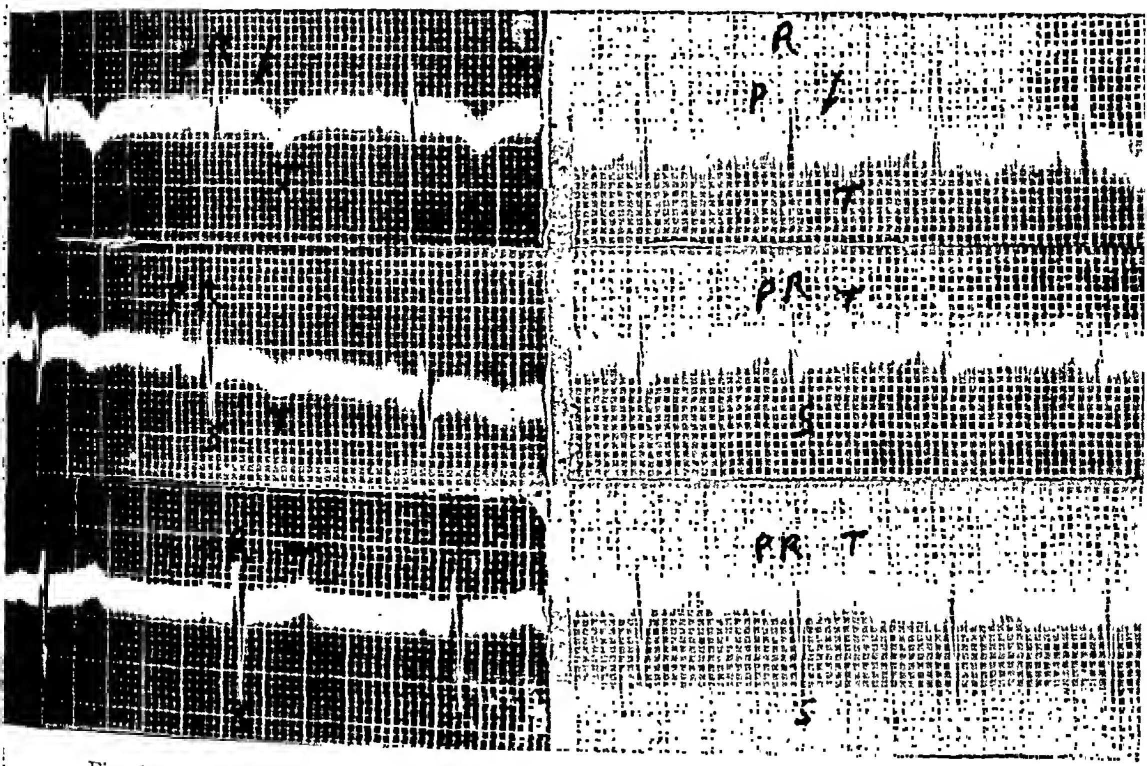

Fig. 1.—Records of two patients suffering from arteriosclerosis of the coronary arteries with the anginal syndrome appearing on effort. The upwardly convex portion of the R-T interval is indicated by the arrows.

early fibrous change with moderate cellular exudate. The left coronary artery is distinctly thickened and has an irregular subintimal proliferation. The fat around the coronary has a marked inflammatory reaction, especially beneath the epicardium. This reaction is focal, plasmocytic and lymphocytic in type. There are a few typical Aschoff bodies. The small blood vessels show moderate thickening, and there are occasional Aschoff bodies in their neighborhood. The wall of the left auricle is thickened, and there is subintimal proliferation with a mild inflammatory reaction in the outer portion of the left auricle. In the neighborhood of the pulmonary artery the pericardial reaction is very marked, becoming practically diffuse, and containing a great deal of hemorrhage. Small focal accumulations have lymphocytes, plasma cells and polynuclears interspersed by Aschoff cells. In addition there are Aschoff bodies. The muscle lying beneath this area shows several regions of inflammatory reaction and foci of early scar tissue formation."

Case 2.—A man, 23 years old, gave a negative history for rheumatism in the past, and had had tonsillectomy two and a half years before because of frequent attacks of tonsillitis. He had been ill at home for a month, with sharp pains over the precordium, and weakness, but had not had to go to bed on this account. He was admitted on January 7, 1927, complaining of palpitation and weakness. On admission the temperature was 100° F., the pulse 82 and respirations 28. He was thin but did not appear particularly ill. His heart showed the cardiac dulness to extend 3 cm. to the left of the midclavicular line. The apex beat was not felt. The heart sounds were distant, and there were no murmurs heard. The systolic blood pressure was 100 mm. The Wassermann reaction was negative. The x-ray examination showed that the heart shadow was of triangular shape, suggesting pericardial effusion. An electrocardiogram taken on January 11 can be seen in Fig. 3. It shows the P-waves of low voltage. The auriculoventricular conduction time is normal, P-R measuring 0.18 second. The QRS group shows no special

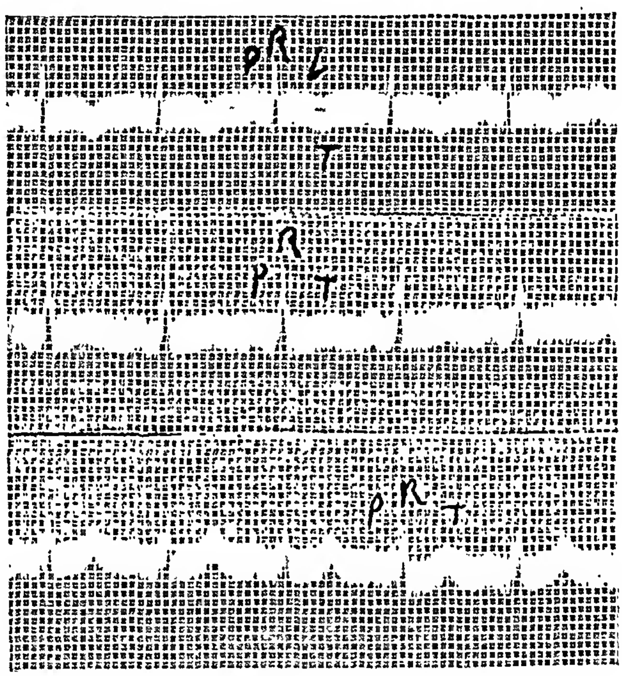

Fig. 2.—Record of Case 1.

abnormality. The T-wave is downward in Leads I and II, and in both leads there is an upward convexity of the R-T interval, like that seen in Figs. 1 and 2. A record taken on January 19 shows essentially the same characteristics as the earlier record. The upward convexity in Lead I is definite, and there is a slight degree of the same appearance in Lead II. During his stay in the hospital his afternoon temperature was frequently above 99° F., and occasionally above 100° F. He remained in the hospital thirteen days, and left against advice feeling well.

Case 3.—A young man, 27 years old, was admitted on January 25, 1928. He had not been sick before this illness. Three weeks before he had felt weak and had had pain and swelling in the left knee, pain over the precordium and fever. On admission he appeared extremely sick, was short of breath and pale. His heart was enlarged to percussion, both to the right and left of the normal area. The rhythm was regular and the rate 94. The temperature was 103° F. There was a pericardial friction rub heard at the apex. The liver was felt 4 cm. below the costal margin. There was an acute polyarthritis involving several joints of the

extremities. The pericardial friction rub varied from time to time but disappeared completely after two weeks. He continued to have an up-and-down temperature. On February 28 he had a severe pain over the precordium, and at that time a systolic murmur was heard at the apex and a split second sound. At the aortic area a blowing diastolic murmur was heard. An electrocardiogram taken at this time is reproduced in Fig. 4. Frequent premature beats are seen, arising from the auriculoventricular node. The auricular waves (P) are normal. The auriculoventricular conduction time is normal; P-R measuring 0.18 second. The QRS group shows a slurring in Leads I and II, and a notching in Lead III. The T-wave is downward in Lead I and diphasic in Lead II, and in both of these leads there is an upward convexity of the R-T or S-T interval, which is similar to the appearance in Fig. 1.

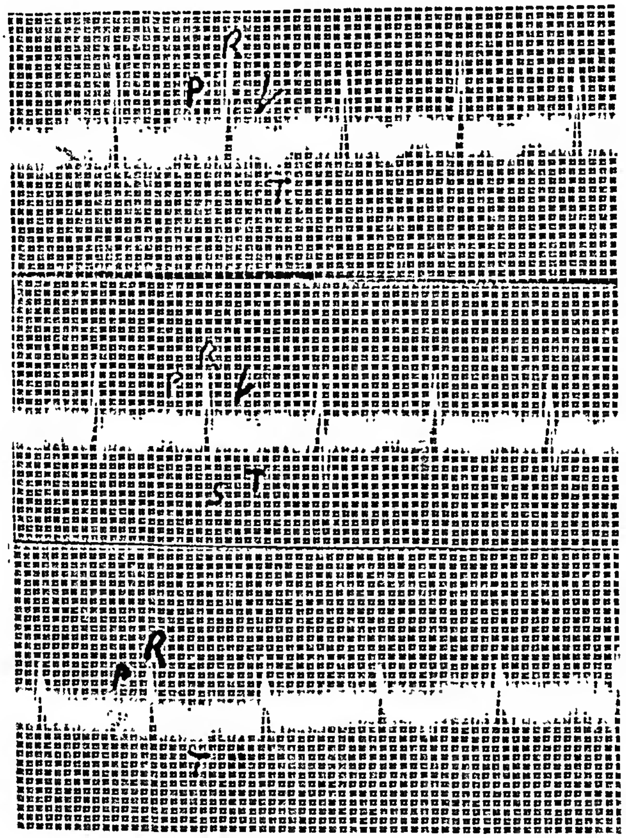

Fig. 3.—Record of Case 2.

Under antirheumatic treatment the fever gradually came down and the patient improved, until by March 21 he was free of symptoms. The electrocardiogram taken on March 26 is seen in Fig. 5. It will be noted that the QRS group is essentially the same, the nodal premature beats still are present, but that the T-wave is now upward in all three leads.

DISCUSSION

These three patients were all suffering from acute rheumatic pericarditis and myocarditis. In the first and third cases an endocarditis also was present, though in the first case it was not recognized during life. The abnormality of the T-wave, or rather of the R-T interval, observed in each of these cases is of special interest. The upward convexity of

this portion of the curve is very similar to that found in the records of certain patients who have had thrombosis of a coronary branch or who are suffering from marked coronary narrowing. Records showing this change in the T-wave, associated with coronary disease, have been reported by several investigators,[2] but in most of the reported records the voltage of the T-wave is greater than that shown in these three cases of rheumatic pericarditis. Occasionally, however, patients with coronary disease give records showing the upward convexity of the T-wave, and also a low voltage of the T-wave, so that from the electro-

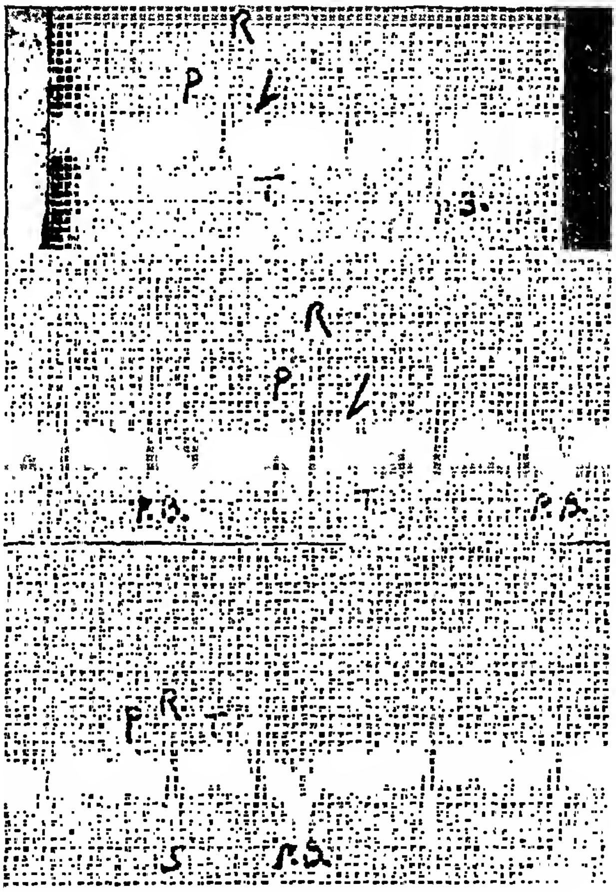

Fig. 4.—Record of Case 3 during the acute stage.

cardiogram alone it would be impossible to diagnose the condition from which the patient is suffering.

We believe that the T-wave abnormality observed in these three cases of pericarditis is due to a complicating myocardial inflammatory reaction. This indeed was found in the case which came to autopsy. We believe that this reaction gives rise to the change in the electrocardiogram, just as the myocardial degeneration, which results from coronary narrowing, produces a similar change in the records of patients with this condition.

It is to be noticed that in Case 3 the peculiarity of the T-wave had disappeared at the time of the second record, giving place to one which was almost if not quite normal. This return to a normal T-wave took place when the patient had clinically recovered from the rheumatic attack and probably indicates that the rheumatic process in the myocardium had subsided.

Changes in the T-wave and in the R-T interval have been reported as occurring in the course of acute rheumatic fever by Cohn and Swift;[3] by Rothchild, Sacks and Libman,[3] and by others. It has not, however, been noted that an upward convexity of the R-T interval like that found after coronary narrowing or occlusion may also occur as a result of rheumatic, myocardial affection. In Fig. 8 *a*, of the article

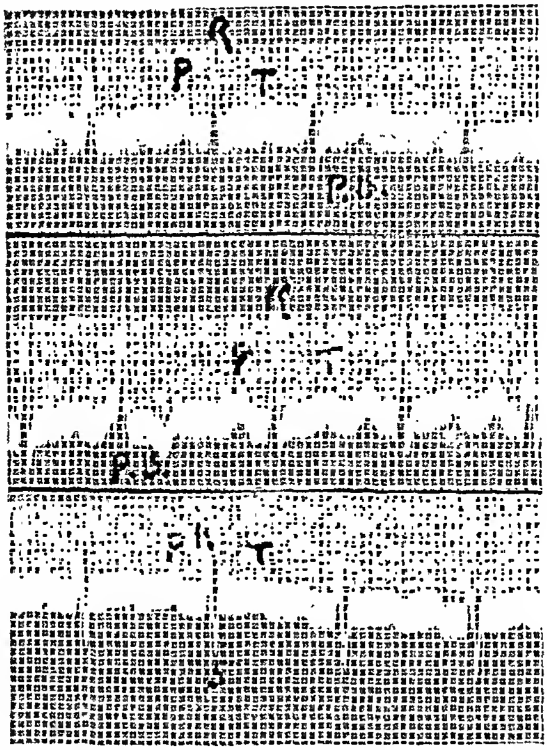

Fig. 5.—Record of Case 3 after recovery.

by Cohn and Swift (patients with rate 102 and 107 respectively), there are two tracings which show this feature; and one of them (rate 107) shows in addition a considerable voltage of the T-wave. It does not appear in this article, however, to which cases these tracings belong, so that we cannot say whether or not these patients had pericarditis.

The similarity of the T-wave in these two conditions, whose pathology is so dissimilar, throws an interesting light on the mechanism of alterations in the form of the T-wave. The fact that quite dissimilar pathological changes may affect the T-wave similarly is not at all discordant with our present understanding of this wave, for it is likely that the location of the damage is of more importance than the damag-

ing agent. It would be interesting if pathological studies should show that a certain location of the disease will cause these changes in Lead I, and that a different location will affect Lead II. So far we have been unable to substantiate this, because of inability to make a sufficiently detailed study of the heart to demonstrate in what areas of the ventricular musculature the disease is most intense. It does not seem unlikely that similar T-wave changes may occur as a result of acute rheumatic myocarditis without the complication of pericarditis, and studies are in progress to elucidate this fact.

We wish to express our thanks to Dr. Orrin S. Wightman and to Dr. Peter Irving for the privilege of reporting these cases which occurred on their services at the city hospital.

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THE AURICULAR BLOOD SUPPLY IN THE DOG

I. General Auricular Supply With Special Reference to the Sino-Auricular Node*

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ALTHOUGH much experimental work has now been done on the specialized tissues of the dog's heart, the blood supply to these structures has never been very carefully investigated. Information of this kind became necessary to us in the pursuance of a physiological problem involving a reduction in the blood supply to the sino-auricular node. The present observations were made in this connection.

The coronary supply to the ventricular portions of the heart has long been a subject of detailed study. The auricular portions have, however, been generally neglected. The full significance of the vascular distribution to the auricles was realized with the discovery of the sino-auricular and atrioventricular nodes. Of all those who have worked on the coronary circulation since that time the most outstanding and the only ones to whom we need specifically refer are Keith and Flack,[2] Koch,[3, 4] Gross,[1] and Spalteholz.[5] In the monograph of Spalteholz a complete bibliography may be found.

As far as the sino-auricular node is concerned these workers completely agree on only one point, namely, that the node has its own special nutrient artery. As to the branches of the coronary which supply this sino-auricular artery, there is much divergence of opinion. In this discussion the terminology of Spalteholz will be used since it is comprehensive enough to include all the arteries described by the other workers. Spalteholz recognizes three main branches to each auricle which arise from the respective coronaries. Each of these branches is termed ramus atrialis, dexter or sinister, and specifically anterior, intermedius or posterior according to its proximity to the origin of the coronary itself.

Keith and Flack, who first described the sino-auricular node, note in man a sino-auricular arterial circle surrounding the superior caval funnel. The portion of this lying in the sulcus terminalis supplies the sino-auricular node. This circle is developed from the ramus atrialis dexter anterior and the ramus atrialis dexter intermedius. There is also an anterior anastomosis with a branch of the left coronary, very evidently the ramus atrialis sinister anterior.

According to Koch also there is an arterial circle around the superior caval funnel which is developed from two branches of the right coro-

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nary. An ascending branch mesial to the right auricular appendage sends a small twig to the appendage caval angle, while the main branch passes around the superior vena cava reappearing on the dorsal surface of the right auricle and entering the sulcus about where the stem of the sinus node ceases. Here it joins a branch of the right coronary which has come up the dorsal wall of the right auricle. The united branches penetrate the sinus node as the sinus node artery. It is evident that Koch is describing the course of the ramus atrialis dexter anterior and the ramus atrialis dexter intermedius. Whether or not the ring is entirely closed by an anastomosis between the sinus node artery and the small twig which passed through the appendage caval angle is not clear. In his later description Koch notes that the mesial branch usually makes anastomoses with branches from the left coronary.

Gross finds with great constancy an arterial ring around the superior caval funnel, and the vessel from which it arises he terms the ramus ostii cavae superioris. This vessel may arise in 60 per cent of the cases as a stout branch of the right coronary soon after its origin, in which case we recognize it as the ramus atrialis dexter anterior. In 40 per cent of the cases Gross finds it originating from the left coronary, very evidently as the ramus atrialis sinister anterior. Although Gross mentions that his ramus ostii cavae superioris when arising from the left coronary may anastomose after reaching the external surface of the right auricle with other auricular branches, he states that there are never two rami ostii cavae superiores, which seems to indicate that he does not believe the sino-auricular node itself is ever directly supplied by anastomoses from both coronaries.

In a series of twenty human hearts figured in his monograph Spalteholz finds a sino-arterial ring in only six cases. In only one of these does the ring receive a branch from the other coronary, such as described by Keith and Flack. In four cases the ring is formed by branches of the left coronary and in two cases by branches of the right. Five times the sino-auricular node is supplied by the ramus atrialis sinister anterior, three times by the ramus atrialis sinister intermedius, nine times by the ramus atrialis dexter anterior and twice by the ramus atrialis dexter intermedius.

METHODS

Although the course of arteries in a limited region may be best studied by serial sections, these are not suitable for following the origin and distribution of entire coronary branches. For this purpose there is apparently no substitute for some kind of an injection method. We have followed the technic of Gross rather closely, using the barium sulphate injection mass. After rigor had passed off, the hearts were thoroughly washed through the coronaries with normal saline. Both washing and injection were done under 150 mm. to 160 mm. Hg. pres-

sure and in a chamber kept at approximately 37° C. Keeping the heart warm during the period of injection was a matter of greatest importance. After the injection was complete, the heart was chilled in cold water and then placed in formalin. Dehydration was brought about by alcohols of increasing strength, the specimens being left in absolute alcohol for several days. Clearing took place in synthetic oil of wintergreen. In the dog the left coronary divides into its two main branches so soon after leaving the aorta that often a cannula was inserted into each branch. By means of Y-tubes all three injection cannulas were then connected to the single pressure bottle.

Our first intention was to study the specimens by means of x-ray pictures. It was soon evident that this was a difficult procedure in the thin walled auricles. From the x-ray pictures it was impossible to tell whether two vessels branched or merely crossed each other. The injected vessels stood out with such contrast to the eye that we finally distended the auricles with strips of dark colored cloth, inserted through the vena cava and tips of the appendages, and made our observations with the binocular microscope. A magnification of from 10 to 20 times brought into view all vessels with their branches and anastomoses down to the smaller arterioles. After becoming familiar with the technic of injection our preservations were uniformly clear and beautiful.

Whitten[6] has recently critically reviewed the injection methods for study of the coronaries. Whatever objections there may be to these methods as applied to the heavy walled ventricles they are eminently satisfactory for the thinner auricles.

THE AURICULAR BLOOD SUPPLY

The distribution of the coronary branches to the auricles may be seen in Figs. 1 and 2. These figures somewhat diagrammatically represent the auricular blood supply as found in 39, or 73 per cent, of 53 dog hearts. The terminology and scheme of numbering used by Spalteholz has been retained but extended where necessary. A brief description of the main branches of each coronary follows.

Ramus atrialis dexter anterior.—This branch (3 in Fig. 1) arises from the right coronary soon after the latter's origin from the aorta. In 49 of our 53 cases it has what Spalteholz terms a weak development; that is, it passes upward over the aortic surface of the right auricle and then distributes itself principally to this region and to the aortic surface of the right appendage. It never anastomoses with any of the other branches which adjoin and somewhat penetrate its territories. This ramus often passes over the margin of the appendage and supplies some of its dorsal and lateral surfaces.

In almost all our specimens another strong branch arises either close to the aorta (3a in Fig. 1) or directly from the right anterior as indi-

cated by the dotted lines in Fig. 1. We have called it the right anterior accessory. It curves around the aorta, supplying the immediately adjacent areas, and then passes transversely across the anterior surface of the right auricle. Some of its branches seem to enter deeply into the interauricular muscular band and so pass on into the septum, although this has not yet been carefully worked out.

In four of the hearts this ramus atrialis dexter anterior accessorius has been very strongly developed. This development is always associated with a very small ramus atrialis sinister anterior. The result is that the accessory branch supplies the entire field ordinarily taken care of by the left anterior. It anastomoses with the right intermedius on both sides of the superior vena cava, sends branches to the areas surrounding the pulmonary veins where it joins branches from the ramus atrialis sinister posterior, and finally it anastomoses with

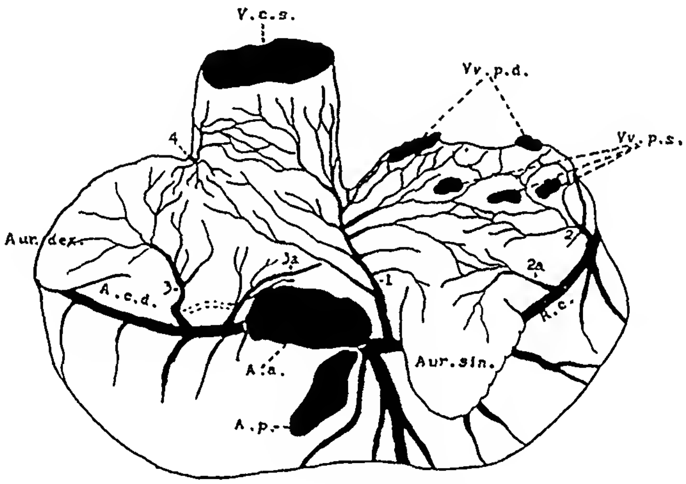

Fig. 1.—Anteroventral view of the auricular regions. The following abbreviations and numbers apply to all figures. V.c.s., superior vena cava; V.c.i., inferior vena cava; Aur. sin., left auricular appendage; Aur. dex., right-auricular appendage; A.c.d., right coronary; R.C., ramus circumflex of the left coronary; Vv.p.s., left pulmonary veins; Vv.p.d., right pulmonary veins; A.a. aorta; A.p., pulmonary artery; 1. Ramus atrialis sinister anterior; 2. ramus atrialis sinister intermedius; 2a. ramus atrialis sinister intermedius accessorius; 3. ramus atrialis dexter anterior; 3a. ramus atrialis dexter anterior accessorius; 4. ramus atrialis dexter intermedius; 5. ramus atrialis dexter posterior; 6. ramus cristae terminalis; 7. ramus atrialis sinister posterior; 8. rami pulmonales sinistri anterioris.

branches from the ramus atrialis sinister intermedius on the anterior aspect of the left auricle. This distribution is so uncommon that it may be termed an anomaly. It is illustrated in Fig. 3.

Ramus atrialis dexter intermedius.—From the right coronary at about the middle of the right auriculoventricular boundary there arises a branch, usually stout, the ramus atrialis dexter intermedius. In 81 per cent of our cases its course is as follows: it first passes transversely across the body of the right auricle then bends sharply forward and finally runs fairly directly to the angle between the superior vena cava and the right appendage. On its way it sends off branches which anastomose with left coronary branches around the right pulmonary

veins. Occasionally its branches extend beneath the inferior vena cava and join arteries from the left coronary in this region. It also sends branches to the left around the superior vena cava which join branches of the left anterior. The main stem transverses the sulcus terminalis and reaches the ventral surface of the auricle by way of the notch between the vena cava and appendage. It does not extend far on the ventral surface but interdigitates with branches of the right and left anterior. In addition it always anastomoses with the left anterior. Sometimes this occurs so directly that it is impossible to say which artery passes from one side to the other. Usually the anastomoses occurs above the sulcus terminalis on the right side of the superior vena cava. Since branches of the right intermediate anastomose with the left anterior on both sides of the vena cava it is

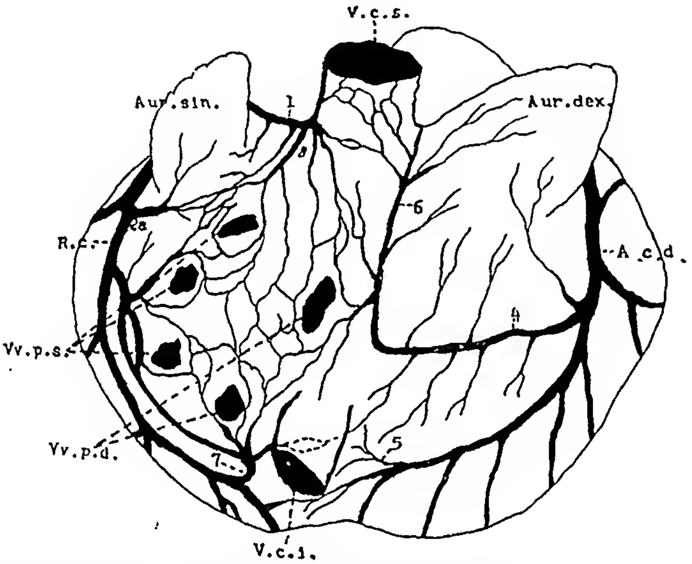

Fig. 2.—Dorsal view of the auricular portions of the heart. The drawing is partially diagrammatic in that the right and left sides have been brought into the same view, somewhat in the manner of a Mercator projection.

obvious that an arterial ring is thus formed around the superior caval funnel.

In forty-three of our fifty-three cases the right intermediate has the above distribution. In all of these it may be said to supply the sinus node since it transverses the sulcus terminalis. Figs. 1 and 2 illustrate the above description.

In eight specimens we have found the right intermediate weakly developed, its place being taken by the left anterior. This condition will be described under that heading.

An unusual development of the right intermediate was found in two hearts. Not far from its origin the artery divided into two large branches, one passing along the sulcus terminalis and through the angle between the superior vena cava and appendage, the other passing between the vena cava and the right pulmonary veins. Both branches thus reached the anteroventral surface where they anastomosed with each other and supplied part of the region usually taken

care of by the left anterior. Anastomoses with the left anterior were also present.

Ramus atrialis dexter posterior.—In the dog this artery is poorly developed and distinguished with difficulty. It reaches the areas on the right side of the inferior vena cava, and under this vein it sometimes anastomoses with branches from the left coronary.

Ramus atrialis sinister anterior.—This branch arises from the ramus circumflexus soon after its origin from the left coronary. It has had a strong development in all except four of our hearts where as already related it was largely replaced by the accessory branch of the right anterior. After its origin the left anterior passes to the left and forward sending large branches to each side of the superior vena cava. It anastomoses freely with the right intermediate usually on the right side just above the vena cava appendage angle and on the left side in

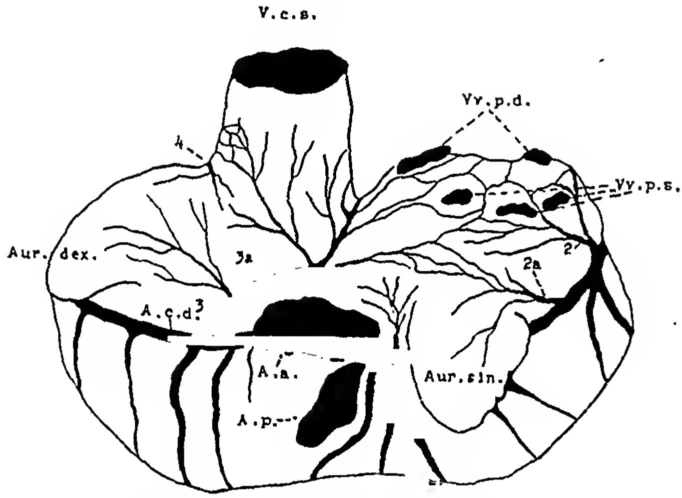

Fig. 3.—Anteroventral view of the auricular regions showing the strong development of the accessory branch of the right atrialis dexter anterior.

the notch between the vena cava and the right pulmonaries. Three or four branches to the left join the plexuses around the pulmonary veins which are made up of branches from the left intermediate and left posterior. There is never any anastomosis with the ramus atrialis dexter anterior. The usual distribution of this artery may be seen in Fig. 1.

In eight of our specimens the left anterior has been unusually strongly developed. The branches that passed to the sides of the superior vena cava extended through to the dorsal surface and supplied the field ordinarily taken care of by the right intermediate including the sinus node itself. There were no anastomoses with the right intermediate on the body of the right auricle, but union did occur in the region of the pulmonary veins. Fig. 4 illustrates the dorsal view of one of these cases.

Ramus atrialis sinister intermedius.—From the lower edge of the left auricle just beyond the appendage two branches arise from the

ramus circumflex of the left coronary, which supply the left appendage and those areas of the left auricle adjacent to the left pulmonary veins. The second of these arteries is usually the larger, and it may be properly called the left intermediate, the first one being conveniently termed the accessory. These arteries may be noted as 2a and 2b on any of the figures. Both the accessory and the intermediate itself anastomose with branches of the left anterior at the base of the left appendage. In the four cases already described in which the left anterior was replaced by the accessory branch of the right antērior there was an anastomosis between this artery and the left intermediates.

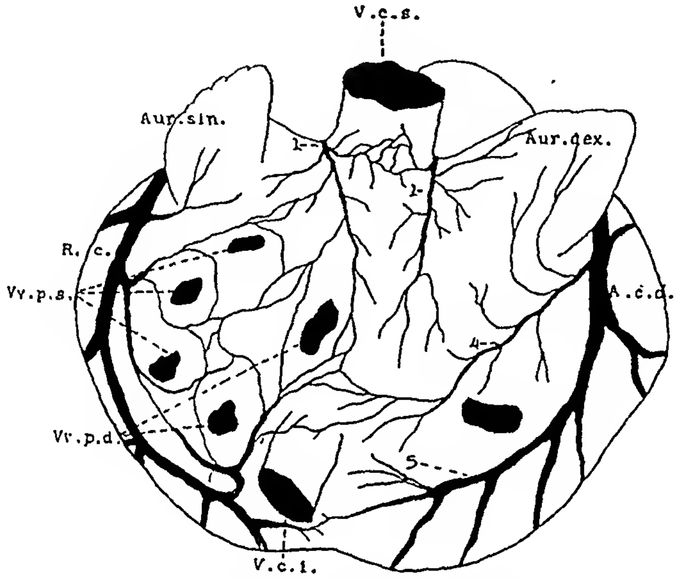

Fig. 4.—Dorsal view of the auricular portions of the heart showing the marked development of the ramus atrialis sinister anterior which has sent two large branches over on the dorsal surfaces. The right intermediate is only moderately developed supplying only part of the right appendage and the lower part of the right auricle.

The left intermediate contributes numerous branches to the plexus of arteries which surround the pulmonary veins. One large branch regularly swings to the right around the base of the left auricle and joins the left posterior. The left intermediate is very regular in its distribution, no variations worth recording being noted in any of our specimens.

Ramus atrialis sinister posterior.—In the angle between the left auricle and the inferior vena cava is regularly found a branch of the left coronary which joins the plexus around the pulmonary veins. It also anastomoses with the right intermediate both on the posterior surface where the two auricles meet and underneath the inferior vena cava. The course of this artery may be seen in Fig. 2.

Ramus cristae terminalis.—This name Spalteholz gives to the artery which penetrates the crista terminalis of the right auricle. In the human heart according to Spalteholz's drawings it was formed nine times from the right anterior, five times from the left anterior, three times from the left intermediate and only twice from the right inter-

mediate. In the dog's heart we have found this artery arising forty-five times from the right intermediate and eight times from the left anterior. Not once has the right anterior passed through the caval appendage angle, as in the human heart, to form this ramus. This artery is numbered 6 in our drawings. The importance of this artery is due to the fact that it lies in the boundary between the sinus and atrium. This region has great physiological significance, for its upper end contains the sinus node. The artery that forms the ramus cristae terminalis, therefore, also supplies the sinus node.

Arterial ring around the superior vena caval funnel.—Keith and Flack emphasized the presenee of an arterial ring around the opening of the superior vena eava into the right auricle. According to their drawings this ring was formed by the right anterior and the right intermediate. Spalteholz found such an arterial circle in only about one-third of his specimens. Three times the ring was formed by the right atrialis sinister anterior, once by the right atrialis sinister intermedius, once by the right atrialis dexter anterior and once by the right atrialis dexter anterior in anastomosis with the right atrialis sinister anterior. We have not found a ring as well marked as indicated in Keith and Flack's drawings, but in all our specimens there is a series of anastomoses around the caval funnel. In thirty-nine cases the ring is formed by anastomoses between the right intermediate and the left anterior as may be seen in Figs. 1 and 2. In eight cases the ring is formed by the left anterior alone as illustrated for the dorsal side in Fig. 4. In four cases the ring is formed by the right anterior accessory and the right intermediate. In two cases the ring is formed by the right intermediate alone. In the dog, therefore, an arterial ring around the caval funnel is constant, and in the majority of cases it is formed by branches from the two coronaries. Even when formed by one artery, somewhere beyond the ring there are invariably anastomoses with other arteries. In Fig. 4 the left branch of the left anterior finally joins the plexus around the pulmonary veins as well as the right intermediate near the inferior vena cava.

Blood supply to the sinus node.—The sinus node is supplied by the right side of the above described arterial ring. The large artery forming this portion of the ring continues as the ramus cristae terminalis. Since the arterial ring is formed either by two separate arteries, or by one artery which later anastomoses with its neighbors, the sinus node is furnished with an abundant and sure blood supply. Preliminary experiments made before the blood supply to the node was known in detail showed that it was extremely difficult to reduce its circulation sufficiently to cause injury. Likewise auricular thrombi are seldom if ever found in the region of the sulcus terminalis. The explanation for both facts is readily found in the anastomosing blood supply.

SUMMARY AND DISCUSSION

By means of barium sulphate gelatin injections the auricular blood supply has been studied in fifty-three dogs' hearts. In forty-five of these the sinus node was supplied by the ramus atrialis dexter intermedius, the second auricular branch of the right coronary. In eight hearts it was supplied by the ramus atrialis sinister anterior, the first branch of the ramus circumflexus of the left coronary.

Although the sinus node artery came directly from the branch just named, there was in all cases studied an arterial ring formed around the superior caval funnel. In thirty-nine cases this ring was formed by anastomoses between the right intermediate and the left anterior, in four cases by anastomoses between the right intermediate and the right anterior, in two cases by the right intermediate alone, and in eight cases by the right anterior alone. In the ten hearts in which a single artery formed the arterial ring there were anastomoses beyond the ring with branches from the opposite coronary. The sino-auricular node could thus always be supplied either directly or indirectly from both coronaries.

The dog's heart has certain regions in which anastomoses do not seem to occur but others in which they are particularly abundant. Of the latter, the superior vena caval funnel has been sufficiently discussed. Fig. 2 shows the rich connections between all the coronary branches that supply the body of the left auricle. The inferior vena caval funnel is very poorly supplied as compared to the superior. There is, however, often an arterial ring made by branches from the left posterior and the right intermediate. The area just ventral to the inferior vena cava in the neighborhood of the coronary sinus is rather well supplied. Anastomoses here occur between the left posterior and right intermediate as well as direct connections between the ramus circumflex and right coronary. Most of these regions have special phylogenetic significance. They are in part boundaries between parts of the heart which have different origins, and in nearly all of them specialized automatic and conductive tissue has been found, either in small scattered masses or in large concentrated nodes.

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THE BUFFER FUNCTION OF THE DIAPHRAGM AND THE CARDIO-ABDOMINO-DIAPHRAGMATIC SYNDROME*

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INTRODUCTION

IN ADDITION to its respiratory function the diaphragm serves as a buffer between the thoracic and abdominal cavities where the pressure is subject to considerable physiological variations. According to A. Bernou,[1] the intra-abdominal pressure varies, not only with the respiratory movements but also with changes in the position of the body. Thus it may vary between 10 and 35 cm. of water during expiration and from 15 to 45 cm. during inspiration, or from 10 to 2 cm. with relaxation of the abdomen.

We shall not consider the extreme variations in intra-abdominal pressure caused by such conditions as pregnancy, tumors, ascites, tympanites, etc., because in such cases the protective function of the diaphragm is of secondary importance. In the ordinary physiological variations in intra-abdominal pressure (variations caused by changes in position, filling the stomach, emptying the intestine, etc.) the diaphragm adequately serves its function of protecting the thoracic organs, especially the organs of the circulatory system, against the harmful effects of variations in intra-abdominal pressure. While the intrathoracic pressure is subject to even more marked physiological variations, caused by respiration and to a lesser extent by the action of the heart, the rôle of the diaphragm in respiration is direct and active. The influence of the respiratory movements of the diaphragm on the abdominal cavity is modified by the combined diaphragmatico-abdominal reflex of Sherrington, that is, by the antagonistic action of the diaphragm and the muscles of the abdominal wall. It is perhaps more accurate to speak, not only of the moderating influence of the diaphragm on the physiological variations of pressure in the abdominal and thoracic cavities, but of a system in which the reciprocal action of the diaphragm and the abdominal muscles is of primary importance. We shall not discuss the question of the part played by the muscles of the thoracic cage, for that is outside the plan of the present study.

The protective action of the diaphragm is the result of variations in the tone of the muscle, and according to Kure, Hiamatsu and Naïto,[2] this tone depends on the sympathetic nervous system, impulses being carried by the splanchnic nerve. That is in accord with the teachings of the school of Prof. L. A. Orbeli[3] that the tone of striated muscles

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depends on the sympathetic system. (See the reports presented at the Congress of Physiologists at Leningrad in 1926.) Similar views are expressed by Backe,[4] de Boer[5] and others.[7] Felix,[6] after extirpation of the sympathetic ganglia related to the diaphragm, observed changes in the latter similar to those met in progressive muscular dystrophy; in the case of complete separation of the diaphragm from the sympathetic system he even observed complete degeneration of the muscle fibers. These findings are in perfect accord with the teachings of Prof. J. P. Pavlov[7] on the trophic function of the sympathetic nervous system. But after all it is hard to believe that the tone of the diaphragm, which functions rhythmically, should depend only on the sympathetic nervous system. According to Frank[10] the parasympathetic system, represented by fibers corresponding to the phrenic nerve, is concerned with relaxation of the diaphragm.

In many ways the function of the striated muscle of the diaphragm seems distinct from that of other striated muscles and in some respects resembles the heart muscle. According to Starling[8] the contraction of the diaphragm lasts from four to eight times longer than does that of any other striated muscle. It seems that this muscle periodically goes into a state of tetany for a short time. If we recall that with respiration the diaphragm maintains a more or less pronounced rhythmic action which continues uninterruptedly throughout life, varying only in degree, we have reason for separating the muscle of the diaphragm, as well as that of the heart, from other striated muscles. We may assume that the tone of this muscle is the result of interplay of the sympathetic and parasympathetic systems. In this connection experiments made by W. M. Bayliss[9] on the effect of cutting the vagus on the tone of the diaphragm are of great interest. It is important to realize, however, that the question of the nervous regulation of the tone of the diaphragm is not finally settled (Kahn[12]).

Frohlich and Meyer[11] speak of a particular tonus system which maintains the tone of the diaphragm directly without being interrupted by ganglia. However that may be, there are reasons for believing that the tone of the diaphragmatic muscle is maintained by the autonomic nervous system and that it must be affected by reflexes from different organs, as the effector link in a whole series of reflex arcs where various organs may serve as receptors. In our observations on the tonotropic reflexes of the heart we have encountered reflexes similar to those of the diaphragm. We have been able to study the following reflexes of the diaphragm:

1. The reflex of filling the stomach (reflex of intragastric pressure).
2. The reflex of pressure on the eyeballs (oculocardiac reflex).
3. The reflex of change from orthostatic to clinostatic position (clinostatic reflex).
4. The x-ray reflex.

METHOD OF STUDY

We did not introduce the roentgenoscopic method in the routine of studying the reflexes, nor did we admit it in our study of the tonotropic cardiac reflexes. The reasons for not using this method are illustrated by Fig. 3 which represents the outlines of the heart and the cardiophrenic angles as determined by percussion, with the patient in the orthostatic position; (1) control, (2) after pressure on the eyeballs and (3) under the influence of the x-rays. From this we see that the effect of the x-ray is similar to that of pressure on the eyeballs, and that the shadow on the screen corresponds with the contour as determined by percussion. The reflex change is seen as a lowering of the diaphragm (determined by the cardiophrenic angles); that is, with these two reflexes there is an increase in the tone of the diaphragm. As the use of the fluoroscope always has this reflex effect on

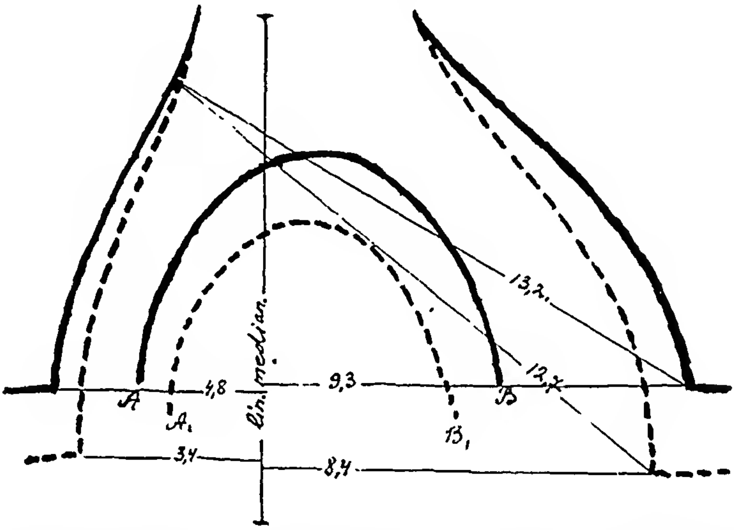

Fig. 1.—Hypotonic dystony of the heart in a man 25 years old with heart failure and dystrophic infantilism. (- - - -) The outline of relative and absolute cardial dullness with the patient at rest in the orthostatic (standing) position. (———) The same with the reflexes (change to clinostatic position, pressure on the eyeballs, fluoroscopy).

the diaphragm, one cannot get a fluoroscopic picture of the height of the diaphragm in the control state, and when the reflexes are already excited by the x-rays, it is only in cases of hyperexcitability of the vegetative nervous system that further reflexes can be elicited. For this reason one must rely on findings made out by percussion.

The determination of the left and right cardiophrenic angles is carried out during shallow breathing when, according to Hofbauer,[13] the central portion of the diaphragm, the heart and even the hilus of the lungs are not involved in the respiratory excursions. Determination of the position of the dome of the diaphragm by percussion is unreliable, and for our purposes percussion of both cardiophrenic angles is sufficient. The percussion is carried out finger-to-finger with quick strong taps as in defining the outline of relative cardiac dulness. We

checked the accuracy of this by comparing the contours determined by percussion under the influence of the x-ray reflex with the shadow on the screen, taking care to have the patient in the same position each time.

THE DIAPHRAGMATIC REFLEXES

In the case of healthy young persons with stable vegetative nervous systems, the tonotropic reflexes of the heart and diaphragm are either absent or insignificant, indicated by an excursion of not more than 0.5 cm. When present the reflex is always expressed as a lowering of the cardiophrenic angles, that is as an increase in the tone of the diaphragm.

We believe that this moderate hypertonic reflex, which occurs when the intragastric pressure is raised, is the normal protective reflex, an evidence of the immediate protective function of the diaphragm. Pres-

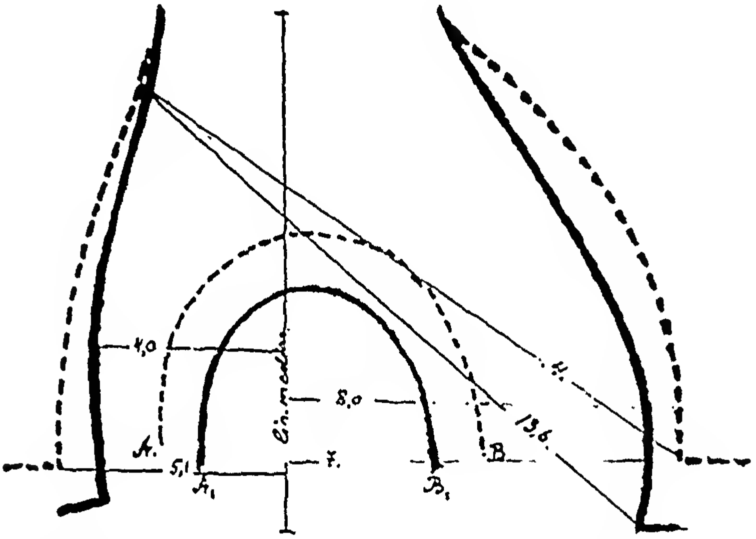

Fig. 2.—Dystony of the heart in a woman 25 years old with dystrophic infantilism. Outlines of the heart in clinostatic position, (_ _) before and (——) after pressure on the eyeballs.

sure on the eyeballs gives a reflex exactly similar to that caused by filling the stomach, even in cases where the rhythmic reflex of Dagnini-Aschner is absent.

This hypertonic tonotropic reflex of the diaphragm is often associated with a hypotonic tonotropic cardiac reflex (dilatation of the heart); that is to say, pressure on the eyeballs often increases the volume of the heart (negative tonotropic reflex) and at the same time lowers the diaphragm (positive reflex). This association is so frequent that we may assume that there is an antagonistic correlation between heart and diaphragm as well as between diaphragm and abdominal muscles.

This type of hypertonic reflex of the diaphragm is still more pronounced in persons with hyperexcitability of the parasympathetic system, especially in young persons with traits of dystrophic infantil-

ism. In such cases the changes already described as occurring in normal individuals are present but to a greater degree; the amplitude of the displacement of the cardiophrenic angles increases to 1 cm. or more, but the reflex still keeps its defensive character (Fig. 1). The most exaggerated type of reflex is seen in cases of spasmophilia and particularly in bronchial asthma.

The conditions change when the general picture becomes complicated by insufficiency of the diaphragmatic muscle followed by a high position of the diaphragm. As the dilated heart muscle can still respond to tonotropic reflexes of contraction or relaxation according to the state of the vegetative nervous system, so can the diaphragm which has lost its tone still maintain the protective type of tonotropic reflex. If there is a change in the relation between the heart and the diaphragm, particularly in cases of dilatation of the heart and permanent

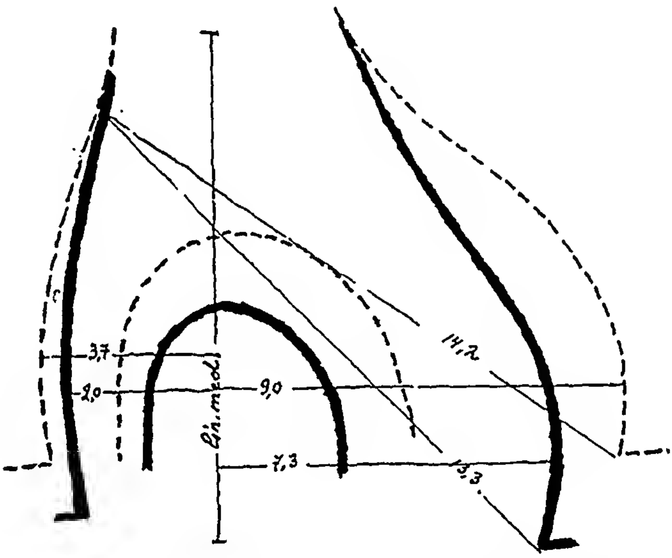

Fig. 3.—Hypertonic dystony of the heart in a man between 30 and 40 years old who had palpitation on exertion. (- - - -) at rest. (——) with the reflexes.

weakness of the tone of the diaphragmatic muscle, this defensive type of reflex may turn against those organs, principally the heart, which it has thus far protected. When there is functional insufficiency of the diaphragm in the presence of considerable cardiac enlargement, the heart pushes down the central portion of the diaphragm forming a deep depression, from the sides of which the two halves of the diaphragm rise quite abruptly. The hypertonic reflex of the diaphragm, increasing the tension of the latter, tends to decrease the inequalities of surface, lowering the domes and raising the central portion on which the heart rests. In other words, the hypertonic reflex is no longer purely defensive but has acquired an active aggressive character. This explains the complaints of patients who, having conserved the hypertonic diaphragmatic reflexes, suffer from aggravation of their symptoms—heaviness, breathlessness, palpitation—after eating, etc.

With loss of tone, however (diaphragma molle or relaxata), the diaphragm may take on an opposite type of reflex, may respond to stimuli by relaxation. The degree of loss of tone may vary according to the general state of the patient, especially according to the degree of fatigue. Altschul observed cases of relaxation of the diaphragm in which this was shown by the level of the domes being higher at night

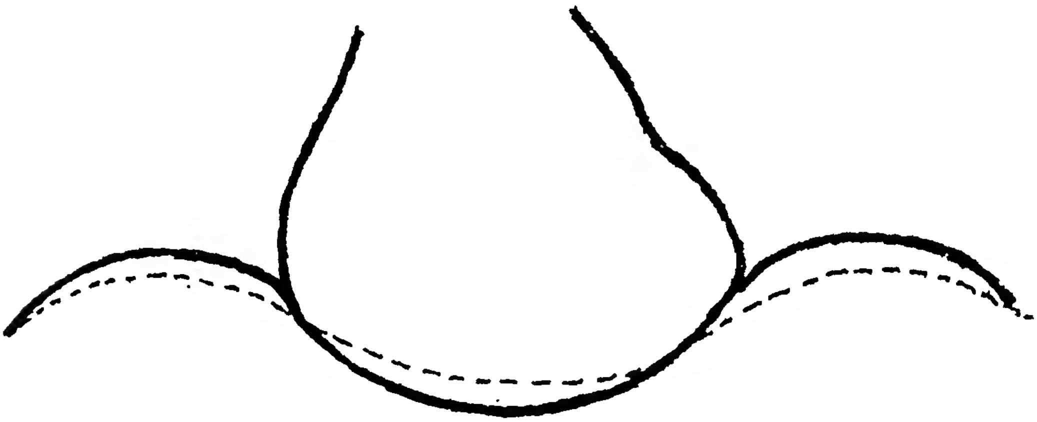

Fig. 4.—Diagram illustrating relaxed diaphragm and enlarged heart.

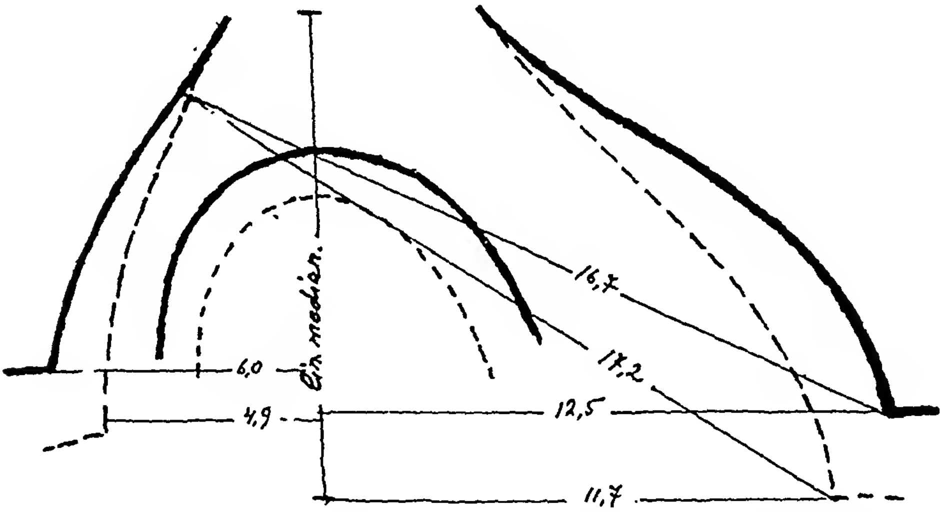

Fig. 5.—Cardiodiaphragmatic syndrome. Patient, a woman, 39 years old with dystrophia adiposo-hypogenitalis, heart failure, and sympatheticoerises affecting the heart, stomach and intestines. Outline of cardiac dullness with patient (- - - -) standing, and (———) sitting.

than in the morning. We do not know whether he considered the possibilities of various reflexes, such as filling the stomach.

As long as the diaphragm maintains its ability to counteract abdominal pressure, that of the stomach particularly, even considerable distention of the stomach does not affect the level of the diaphragm. Altschul,[14, 15] after x-ray studies, came to the conclusion that there was no definite relation between the height of the diaphragm and the degree of distention of the stomach. In another paper the same author

mentions a case in which filling the stomach or distending it with gas caused no displacement of the left hemidiaphragm.

When the muscle is hypotonic, one might expect that the decrease in intra-abdominal pressure resulting from the high position of the diaphragm and the relaxation of the abdominal wall would predispose to the accumulation of gas, would permit an increased amount of gas to collect in the stomach and intestine. In other words a collection of gas is not necessarily primary but may be secondary.

With decreased tone of the diaphragm, change in the autonomic balance in the direction of decreased excitability of the parasympathetic system, and the development of a whole series of sympatheticotonic symptoms,* the protective function of the diaphragm is greatly disturbed.

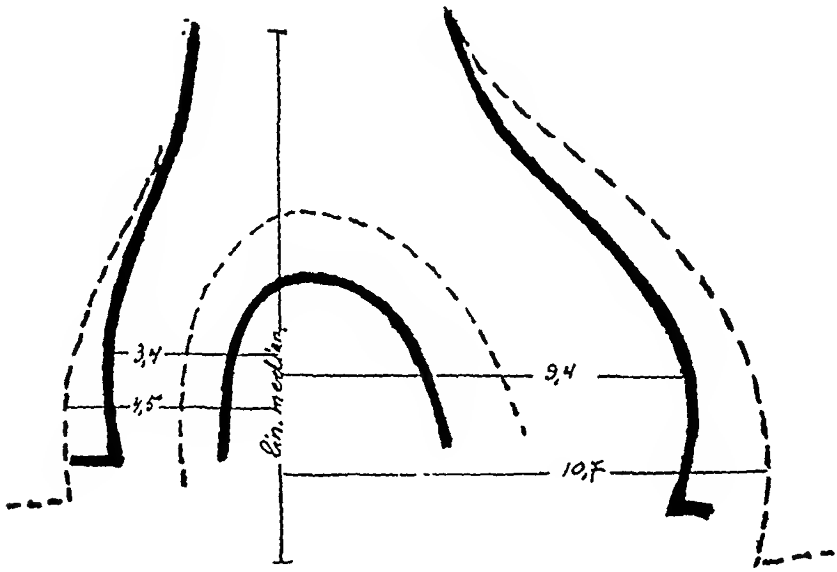

Fig. 6.—The effect of the injection of embryonal extract on the outline of the heart. (- - - -) control, (—) after injection.

Perversion of the function of the diaphragm alone ordinarily gives rise to no symptoms as long as the functions of the organs it protects are normal, as long as the heart is strong enough to overcome unfavorable conditions of work. According to Healy,[16] of 53 cases of relaxed diaphragm 47 were discovered accidentally by x-ray. But relaxation of the diaphragm followed by functional insufficiency of the organs which it normally protects, of the heart for example, is evident at once.

*We do not apply the term, "hypersympatheticotony" to the development of sympatheticotonic symptoms accompanying the ageing process, because we are not sure that the sympathetic system is not involved in this process, and that it is not subject to qualitative as well as to quantitative changes in its functions. Without disregarding the multiplicity of the functions of the sympathetic nervous system, we may remark that one function, trophic, is definitely disturbed as the organism grows old.

INSUFFICIENCY OF THE DIAPHRAGM

Insufficiency of the diaphragm with reference to its protective function can easily be determined by comparing its height with the patient standing and sitting. When the function is good, the level does not change perceptibly; but when it is insufficient, one gets another picture as is illustrated by the following case from the Out-Patient Department of the Polyclinic Tzekoubou.

A woman, 54 years old, was examined October 5, 1927. She presented evidence of dystrophia adiposogenitalis, had a relaxed flaccid abdomen, and complained of dyspnea and painful sense of distention of the upper part of the abdomen. She had not menstruated since an oophorectomy in 1908. The diaphragm was more than 2 cm. higher when the patient was sitting than when she was standing. From this it resulted that, in spite of the relaxation of the abdominal wall and the absence of increased abdominal pressure, the diaphragm and the abdominal press

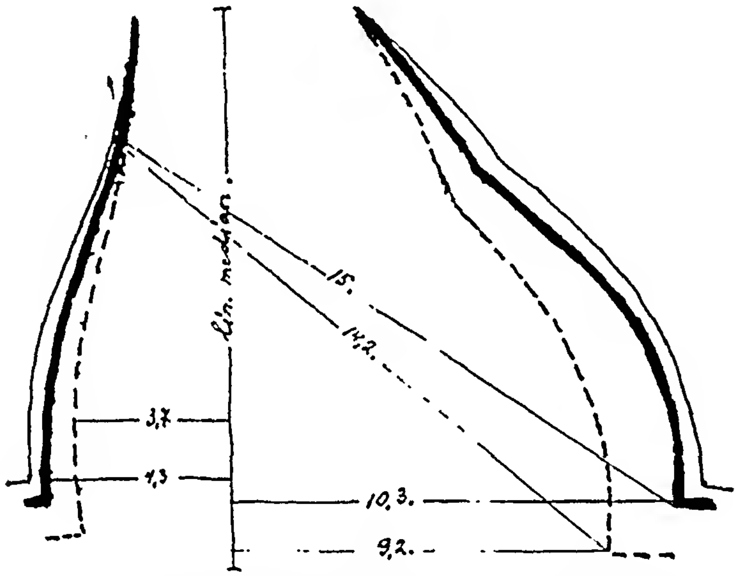

Fig. 7.—The effect of the injection of 1 c.c. of adrenalin, 1:1000; (——) control, (- - - - -) immediately after the injection, (——) 24 hours later.

having lost their protective function did not give physiological correlation between intra-abdominal and intrathoracic pressure and caused the development of a cardiodiaphragmatic syndrome. (For similar case see Fig. 5.)

Adipose dystrophy is not necessary for the development of the cardiodiaphragmatic syndrome. Patient K, for example (seen in office consultation) was a mechanic, 31 years old. He was thin. He had mitral stenosis which had followed an attack of acute rheumatic fever when he was 14 years old. Blood pressure was 134/84 mm., oscillometric index 12 m/n. He complained of dyspnea and palpitation after meals and particularly after heavy meals. Comparison of the level of the diaphragm with the patient sitting and standing showed that it was much higher in the former position.

Especially when patients with cardiac disease complain of malaise after meals, change of position, etc., we find more or less marked evidence of functional insufficiency of the diaphragm. The syndrome is the more serious when there is excitability of the visceral nervous

system. Nevertheless, the cardiodiaphragmatic syndrome, that is the development of a series of symptoms (palpitation, dyspnea, pain) due to elevation of the diaphragm resulting from its functional insufficiency (after eating or drinking, when sitting or lying down), is most frequently seen in persons with adipose dystrophy. It is most often seen in young persons with hypopituitary dystrophy and underdevelopment of the genitals (dystrophia adiposo-hypogenitalis), at the menopause or after oophorectomy, or in either sex with disturbance of the gonads. It is often associated with early sclerotic changes in various organs and a more or less marked functional insufficiency of the heart. Decreasing tone of the diaphragm, dilatation of the heart, deposit of abdominal fat, weakness of the abdominal muscles, and atony of the digestive tract are the factors which favor the appearance of the cardiodiaphragmatic syndrome. It is possible that distention and stretching of

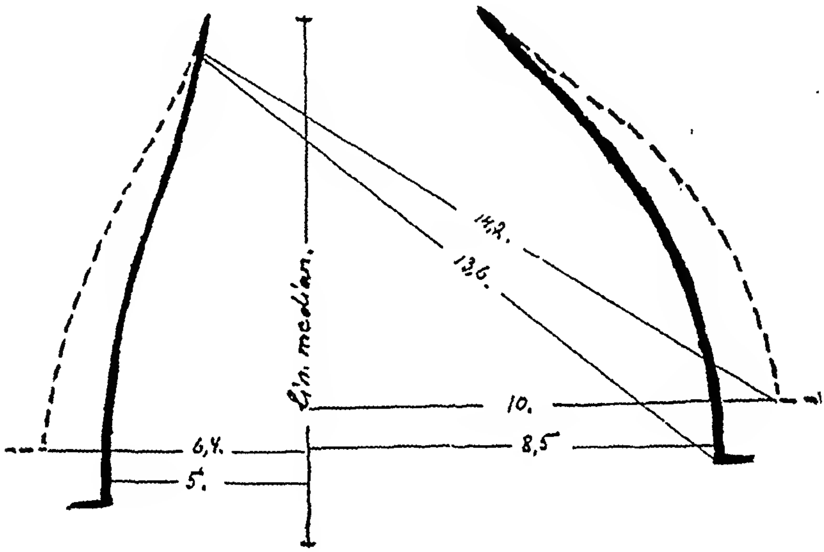

Fig. 8.—The effect of the injection of 1 c.c. of sodium nitrite, 10 per cent; (—) control, (- - - - - -) after the injection.

the walls of the intestine may set up nervous stimuli affecting the heart and the diaphragm.

The experiments of Pearcy[17] are interesting in this connection. He showed that reflexes from the abdominal viscera (distended intestine, gall bladder or urinary bladder) had no effect on the hearts of healthy animals, but that a reflex was always demonstrable in cases in which a toxic myocarditis had been produced experimentally. Thus there is experimental evidence that the healthy heart is not markedly affected by stimuli from the abdominal organs, but that a diseased heart becomes the target for such stimuli.

One must assume that the heart, the diaphragm and every other organ may be influenced by pathological tonotropic reflexes from other organs under the following conditions, disturbance of the effector organ, hyperexcitability or unbalance of the visceral nervous system,

or functional disturbance of the receptor organ. In vagotonic cases these tonotropic reflexes are expressed as dilatation of the heart and increased tone of the diaphragm, but in such cases the rôle of the diaphragm is of minor importance. In sympatheticotonic cases the tone of the heart is increased while that of the diaphragm is decreased, giving rise to the discomfort of the so-called sympatheticotonic cardio-diaphragmatic syndrome, in which the cardiac symptoms are prominent and the rôle of the diaphragm is essential.

From this description of the syndrome we omit to mention the respiratory disturbances, for these probably bear no immediate relation but are produced by circulatory and anoxemic disturbances of the respiratory center. Indeed, there may be disturbances of other organs in this cardio-abdomino-diaphragmatic syndrome, but the factors of the heart, the diaphragm, the abdominal press, and the nerve tonus are of fundamental importance. In diagnosing and interpreting the mechanism of the syndrome none of these factors should be considered alone, for only by taking all together can the syndrome be understood.

TREATMENT OF THE CARDIO-ABDOMINO-DIAPHRAGMATIC SYNDROME

While symptomatic treatment may give satisfactory results, it is only by considering more broadly the mechanism of the syndrome that we can determine the possibilities of rational treatment.

In recent years we have found that in cases of cardiodiaphragmatic and abdominovisceral syndrome based on dystrophia-adiposo-hypogenitalis good results may be obtained from the injection of 1 c.c. of pituitrin, two, three or four times weekly, combined with daily injection of glandular extracts depending on the sex of the patient (ovarian, testicular, spermine, etc.). At times, when the picture is complicated by hypothyroidism, we give thyroid extract by mouth once or twice daily, regulating the dose by the indications of the individual case. While there can never be a complete restoration of the normal state, in the entire series of cases symptomatic improvement was the rule. Attacks caused by the condition became milder and less frequent or disappeared completely; the function of the intestines improved and gaseous distention disappeared; the diaphragm became lower; and what is specially characteristic, the painful symptoms of adiposa dolorosa became milder and disappeared. (This is particularly true of women at the menopause.) Among other cases I can cite that of a singer who under this treatment lost 15 pounds, regained the normal function of her diaphragm and was able to move about freely without dyspnea. I have a series of women over fifty years old, who under this treatment lost their discomfort after eating and regained their ability to sleep flat in bed and to lead active lives. One patient, whom

I have observed for almost two years, has even ceased to have anginal attacks.

We have made a number of experiments to determine the possibility of securing a prompt and vigorous effect on the tone of the diaphragm. While strychnine and extracts of the sexual glands have a definite action in such cases, this action develops so slowly that it is difficult to study it experimentally after a single dose.

A single injection of adrenalin, pituitrin or embryonal extract produces a definite effect on the tone of the diaphragm. This is best seen in cases in which there is not great increase in the size of the abdominal cavity, in which the diaphragm is not fixed and in which the abdominal muscles retain their power.

Fig. 6 represents the effect of a single subcutaneous injection of 1 c.c. of embryonal extract in a patient with infantile dystrophy and a high position of the left dome of the diaphragm. After this injection the two cardiophrenic angles were lowered. The following two or three injections served to establish the new level of the diaphragm and to abolish the hyperactivity of its reflexes.

It is true that when the heart is dilated and pressing down upon the central portion of the diaphragm a decrease in the volume of the heart decreases this pressure of the heart on the diaphragm, and an injection of embryonal extract may produce a paradoxical result. For example, the cardiophrenic angles may rise, as we see in Fig. 4 of our paper "The Effect of Embryonal Extracts on the Tone of the Heart Muscle in Cases of Infantilism." Fig. 1 of the same paper shows a similar effect from a subcutaneous injection of 1 c.c. of a 1:1000 solution of adrenalin.

The effect of embryonal extract lasts from twenty-four to forty-eight hours, or even longer, but the effect of adrenalin disappears within from eight to twelve hours, and within twenty-four hours the diaphragm has returned to its original level or is in an even more unfavorable position. Pituitrin is less active than embryonal extract, but its effect lasts longer than does that of adrenalin, and after its use there is never the marked decrease in tone which may be observed after adrenalin.

Sodium nitrite lowers the tone of the diaphragm. It produces dilatation of the heart and decreases the spastic tonotropic reflexes.

Fig. 8 indicates the response to the injection of 1 c.c. of a 10 per cent solution of sodium nitrite. The patient was a laborer, 38 years old, with moderate hypertension, blood pressure 156/90 mm., but without arteriosclerosis. He complained of pricking precordial pain, sense of oppression, dyspnea, and anxiety after fatigue, after meals, when excited, and at night. Subjectively there was considerable relief after the first subcutaneous injection of sodium nitrite, but with this the heart was dilated, both cardiophrenic angles were elevated, and there was no objective evidence

of improvement. Apparently the subjective improvement was produced by the change in the vegetative nervous tone of the heart resulting in dilatation and lessened response to reflexes.

With embryonal extract, pituitrin and extracts of the gonads, we improve the whole condition, but with sodium nitrite we only remove the spastic heart symptoms. It may be useful to remove these symptoms, but we believe the other treatment to be more useful.

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Department of Clinical Reports

TOXIC MANIFESTATIONS OF BARIUM CHLORIDE IN A PATIENT WITH COMPLETE HEART-BLOCK*

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IN RECENT years, the administration of barium chloride has been advocated for the prevention of syncopal attacks associated with standstill of the ventricles in patients with complete heart-block.[1] The basis for the use of this drug depends upon its ability to keep the idioventricular pacemaker in an irritable state and thus prevent ventricular standstill, which in the majority of these cases is responsible for periods of unconsciousness that accompany this type of inactivity of the heart.

The exact dosage of the drug needed to produce the desired effect is still unknown. According to Levine[2] it is probably 30 mg. four times a day, while Herrmann and Ashman[3] have reported "spectacular" results without any detrimental effects from the use of heavy doses over prolonged periods of time. Indeed, in one of their patients the oral administration of a single dose of 20 grains (given by mistake) produced no untoward symptoms save nausea and vomiting and a moderate diarrhea.

The following patient with complete heart-block is of particular interest because after the administration of only 60 mg. of barium chloride, he showed within several hours an irregular acceleration of the ventricles with alarming symptoms of extreme breathlessness and signs of circulatory collapse, all of which cleared up with the elimination of the drug.

REPORT OF CASE†

L. R., male, aged fifty years, a tailor, was admitted to the Montefiore Hospital on August 5, 1927 and died on November 28, 1927. He was suffering from heart failure and complete heart-block and from the time of his admission to the wards he became progressively worse. He was dyspneic and cyanotic; his legs were markedly swollen, and he showed hydrothorax and ascites. In the last few months of his illness he responded very poorly to graded doses of digitalis. Following the administration of approximately 50 c.c. of tincture of digitalis within one week, during a time when he was known to show complete heart-block with a ventricular

*From the Medical Division of the Montefiore Hospital for Chronic Diseases, New York City.

†This case was reported in detail in connection with another phase of therapy, so that only its salient features are given here. *Vide*, The action of Digitalis in Complete Heart-Block, The Am. Heart J. (to be published).

rate of 41 and an auricular rate of 68 beats per minute, the patient developed an irregular acceleration of the ventricles averaging 98 beats per minute, with bigeminal rhythm and auricular fibrillation. These abnormal rhythms were considered toxic manifestations of digitalis and all of them disappeared so that three weeks later there was again complete heart-block with a regular ventricular rate of 41 beats per minuts and an auricular rate averaging 88. (Fig. 1.)

At this time, October 23, 1927 at 9 A.M. when his heart rate was regular, the patient was given two doses of barium chloride of 30 mg. each within four hours.

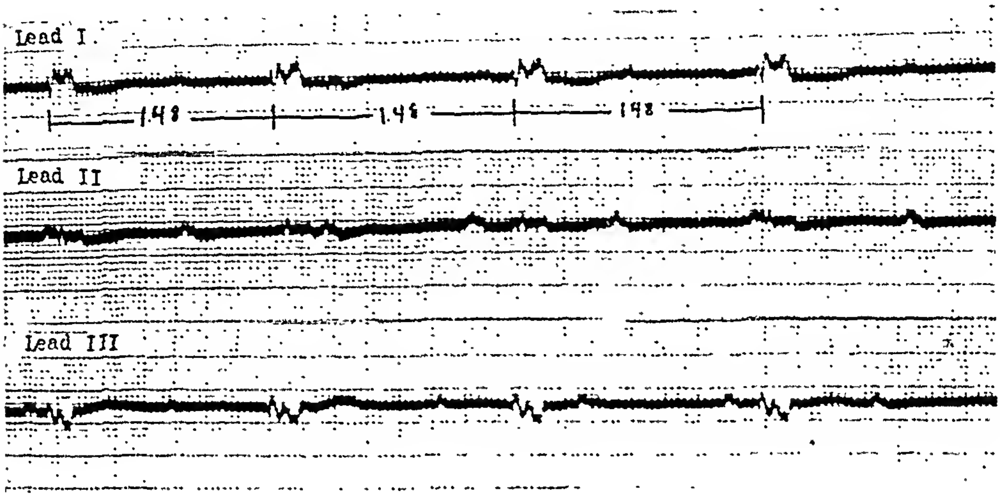

Fig. 1.—Ecg. No. 2844. Complete heart-block before the administration of barium chloride. Ventricular rate 41, auricular rate 88. Note also the intraventricular conduction disturbance (arborization block) i.e., low voltage and prolongation with deep notching of the QRS complexes.

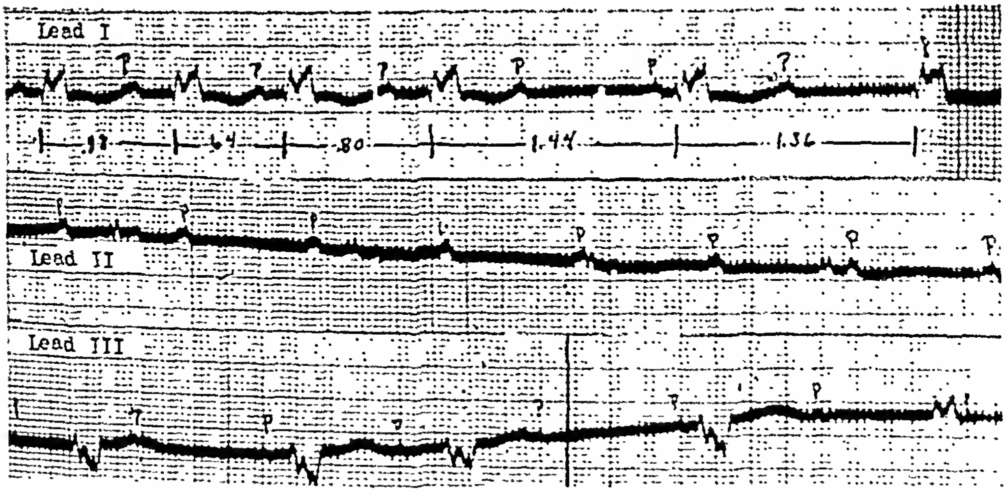

Fig. 2.—Ecg. No. 2974. After the administration of barium chloride. Irregular acceleration of the ventricles. The auricles are not affected.

His general condition preceding this was poor, but he was breathing with ease and he was not cyanotic. His legs were extremely swollen; he showed no signs of fluid in his chest, and there was only moderate ascites.

Following the administration of the last dose of barium chloride, the patient's condition became suddenly worse. He breathed with difficulty and his respirations were irregular. His face became intensely cyanotic and his sensorium was very disturbed. He was disoriented and his speech became unintelligible. For the next

hour it was difficult to arouse him and severe pressure over the supra-orbital nerve just caused him to groan. Large beads of perspiration appeared on his forehead. His pulse was barely perceptible.

Coincidentally with these changes in his symptoms there was noted a very marked irregularity of his heart rate. This was now totally irregular and although there was no pulse deficit, even to the trained observer the rhythm resembled that of auricular fibrillation with an irregular ventricular rate which at times was as high as 93 beats per minute. The electrocardiograms taken at this time showed an irregular ventricular acceleration due to stimulation of the idioventricular pacemaker. The auricles were not affected by this change. (Fig. 2.)

The irregularity of the heart disappeared toward the evening of this day and with the restoration of the dominant rhythm of complete heart-block the patient began to feel much better.

It was impossible to repeat this test, as the patient refused to take any more medication. He died on November 28, 1927 and during the rest of the period of observation, he never showed any irregularities except a complete heart-block.

COMMENT

While, as experience has shown, barium chloride may be a safe drug to prescribe to patients with complete heart-block suffering from Stokes-Adams disease, there is probably a group of cases with auriculo-ventricular dissociation in which the drug produces deleterious effects. It is possible that these patients who are so susceptible to the drug, as in the case reported here, may never show the signs of ventricular standstill and that the response to barium chloride represents in them a highly irritable idioventricular pacemaker. Nevertheless it is important to realize that it does not require much of the barium chloride to produce toxic symptoms in an individual susceptible to the drug. For this reason attention is called to the fact that caution and care must be exercised in the administration of barium chloride to any patient with heart-block.

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A CASE OF PAROXYSMAL TACHYCARDIA IN THE COURSE OF ACTIVE SUBACUTE BACTERIAL ENDOCARDITIS*

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CASE REPORT

C. K., male, 23 years old, was admitted January 11, 1929, complaining of fever, cough, and pain in the right side of the head. The onset of the illness occurred two months before admission, with a cold accompanied by cough and blood-streaked sputum. One week before admission the patient began to feel feverish, had night sweats and developed pain in the right side of the head, left shoulder and left foot.

Family History.—Essentially negative.

Previous History.—Pleurisy and pneumonia four years before. No history of tonsillitis, rheumatic fever or chorea. No history of gonorrhea.

Physical Examination.—The patient was a young adult male, well developed, presenting marked pallor, not exactly of the café au lait type. The conjunctivae showed no petechiae; the ocular conjunctiva was pearly; pupils were equal and reacted to light and in accommodation; eyegrounds negative. Nose was clear; pharynx was slightly injected. No adenopathy. There was slight tenderness at the left subacromial region and at the left ankle. Lungs: slightly impaired resonance at the right apex and left base; no râles. Heart: some increase in the horizontal diameter, especially to the left; presystolic and systolic murmurs at apex with synchronous thrills; the systolic murmur was transmitted posteriorly and was heard down to the second lumbar vertebra; short, coarse, diastolic murmur at the base. Blood pressure 100/70 mm. Spleen: just palpable; slight left para-umbilical tenderness. Liver not palpable. Knee jerks present and active.

Diagnosis on Admission.—(a) Chronic rheumatic cardiovascular disease; (b) mitral stenosis and insufficiency; (c) mitral and aortic valvulitis; (d) subacute bacterial endocarditis.

Subsequent Course.—January 13. Osler node noted on middle finger of left hand.

January 14. Blood culture negative.

January 15. Patient fell and was found to have a left arm paresis and a left supranuclear facial paresis. A petechia was noted in the upper right lid; eyegrounds negative.

January 18. Paroxysmal tachycardia noted, rate 190. Patient complained as usual of pain in right temporal and facial regions and in left loin.

January 20. Paroxysmal tachycardia continued. Patient did not complain of his cardiac condition.

January 21. Left hemiparesis; Babinski sign, positive; ankle clonus present; no petechiae observed. Patient did not complain of his paresis or cardiac arrhythmia. Still distressed about facial and loin pain. EKG paroxysmal tachycardia, rate 188, auricular.

*My thanks are due Dr. Alexander Lambert, Director of the Fourth Medical Division, and Dr. Douglas Symmers, Director of Laboratories, Bellevue Hospital, for permission to report this case from the wards of Bellevue Hospital.
Read before the New York Pathological Society, March 14, 1929.

January 23. Heart rate as before; no subjective or objective evidences of decompensation.

January 24. Rate down. Patient conscious of change of heart rate but unconcerned. Slight neck rigidity; no Kernig.

January 26. Phlebitis of vena mediana cubiti.

January 31. Blood culture positive for Streptococcus viridans after 144 hours. A single white centered petechia noted on right wrist.

February 6. Pustules on left buttock.

February 19. Pain in left loin exacerbated. Diagnosed as infarct of kidney or perisplenitis. No red blood cells found in urine.

February 20. Few râles noted in left axilla.

February 28. Patient vomited early in morning; soon went into coma. Spasticity developed in upper and lower extremities. Right pupil larger than left. Cheyne-Stokes breathing followed.

March 1. Patient died at 4:05 A.M.

During the course of the illness the temperature averaged 102° F. with many fluctuations. The patient received digitalis, aspirin, codein, and occasionally hypnotics.

Post-mortem Examination.—Only positive findings are given. Numerous petechiae of conjunctivae; several petechiae over right shoulder posteriorly; multitudes of petechiae over right and left pleurae. Left hemohydrothorax (over 1000 c.c.). About 300 c.c. of serous fluid in pericardial sac; weight of heart 350 gm. Several petechiae were present in the wall of the right auricle. The mitral valve showed some stenosis. There were verrucous vegetations of this valve, extending to the chordae tendineae and well upwards on the auricular wall. At the cephalic pole of the limbus fossae ovalis there was dusky discoloration of the endocardium, which upon cut section seemed to be a small ecchymosis. One of the leaflets of the aortic valve presented a sessile, flat vegetation from 3 mm. to 5 mm. in diameter. Another of the leaflets showed a large petechia. The liver weighed 1950 gm.; on cut section it was dark red. The spleen was somewhat large, weighing 260 gm., and showed two large infarcts of different age. Both kidneys together weighed 300 gm. The capsules stripped with difficulty, and the surface was somewhat granular; the left kidney showed no other gross abnormality; in the right kidney were numerous infarcts. The brain was not examined. The myocardial petechiae were confirmed by histological study. In the ventricular myocardium there was one large focal accumulation of large mononuclear cells; there were scattered foci of fibrotic change, especially in the myocardium beneath the mural endocarditis.

DISCUSSION

The view commonly held of the infrequency of cardiac arrhythmias in subacute bacterial endocarditis and the pertinent one of an infrequency of myocardial involvement are well expressed by Bickel:[1] "It is remarkable that functional alterations of the excito-conduction system, so frequent in the most diverse general toxi-infections, have been noticed only exceptionally in diseases predominantly localized to the endocardium, such as the septic endocarditides. They seem particularly rare in 'l'endocardite à évolution lente,' and we have not been able to encounter a single case in a rapid bibliographical study." This accords well with the fact noticed by most authors of the rarity of myocardial involvement. Debré tells us in his excellent general review: "The myocardium is slightly involved, the pericar-

dium is intact, besides patients complain little of their hearts and the functional disturbances are inconstant and reduced to a minimum."

Homer Swift[2] says, "Instrumental signs of extensive parenchymatous irritation of the heart are as rare in subacute bacterial endocarditis as are peripheral signs of exudation." Bickel describes a case with heart-block. The only other case with an arrhythmia definitely diagnosed as active subacute bacterial endocarditis that I have been able to find is one of auricular fibrillation reported by Rothschild, Sacks and Libman.[3]

THE MYOCARDIUM

Blumer[4] in a study of 150 cases of subacute bacterial endocarditis found chronic interstitial involvement of the myocardium in 5 per cent (8 cases) and acute myocarditis in a little over 1 per cent (2 cases). Clawson[5] found inflammatory myocardial changes in 24 per cent of 54 cases of subacute bacterial endocarditis. Thayer[6] in a more intensive study found acute myocardial involvement in 60.8 per cent and chronic fibrotic changes in 63.6 per cent of his cases. Considering the generally accepted view of the precedence of subacute bacterial endocarditis by rheumatic fever in which myocardial involvement is "invariable," one should expect a proximate frequency of at least the fibrotic change in subacute bacterial endocarditis. As for the acute inflammatory change, the truth might well be approached by an application of Mackenzie's[7] general dicta: "Another point to bear in mind is that in the invasion of the heart the specific organism rarely affects one tissue alone. In order to be exact and methodical writers usually describe separately the symptoms of endocarditis, myocarditis and pericarditis. But if one reflects on the nature of the symptoms, such as the condition of the pulse, its strength and rate, the size of the heart and the precordial distress—the symptoms which are usually included in the description of endocarditis and pericarditis—it will be realized that they are not really the manifestations of endocarditis or pericarditis but are the signs of a myocardial affection."

The discrepancies in the studies cited and the difference between apparent fact and so valid a supposition as Mackenzie's are strange. From the point of view of diagnosis, prognosis and a better clinical and pathological understanding of the disease, it is essential that these opposing views be correctly estimated. The symptoms, clinical features and pathological findings, each offers a barrier to our knowledge of myocardial involvement in subacute bacterial endocarditis. Clinically, as Debré[8,9] accurately states, "These patients are cachectics, never cardiacs." It is well to remember, however, that peripheral congestive phenomena are not the only evidences of cardiac decompensation. Clinically, also, the anemia and peripheral embolic phe-

nomena are so striking and varied that they attract almost the entire attention of the clinician. This is quite different from the monotonous regularity of the congestive phenomena of chronic cardiovalvular disease where the cardiac signs and close digitalis control become so engaging. Pathologically, the endocardial involvement so obtrudes that we are apt to and really do neglect a more careful study of the myocardium. It is quite probable that when we have pursued our studies of the living and dead myocardium in subacute bacterial endocarditis with the persistence with which we have pursued the presystolic murmur and the Aschoff body in acute rheumatic fever, we shall find little if any percentage disparity of myocardial involvement in these two diseases. The report of this case is a small effort in that field.

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9. Libman, E.: The Clinical Features of Cases of Subacute Bacterial Endocarditis That Have Spontaneously Become Bacteria-Free, Am. J. M. Sc. 146: 625, 1913. (Libman describes 3 of 16 fatal bacteria-free cases where death was due to cardiac decompensation without profound anemia.)

Department of Reviews and Abstracts

Selected Abstracts

Cutler, Elliott C. and Beck, Claude S.: The Present Status of the Surgical Procedures in Chronic Valvular Disease of the Heart. Arch. of Surg. 18: 403, 1929.

This article summarizes the twelve cases of chronic valvular disease of the heart that have been subjected to operation. The cases included one of pulmonic stenosis, one of aortic stenosis and ten cases of mitral stenosis. Of the ten patients with mitral stenosis who were operated upon, one only is living, a mortality of 90 per cent. Eight of the ten patients died so soon after the operation that the changes brought about in the mechanics of the circulation could not be adequately studied. One patient lived four and one-half years after the operation.

There have been three kinds of procedures utilized in the attempts to enlarge the stenotic orifice. These methods are finger dilatation, incision of the stenotic valve and excision of a segment of the stenotic valve.

The authors feel that the twelve cases are not sufficiently numerous to justify conclusions as to the value of the operation nor is it possible to answer certain questions that arise in this connection. The mortality figures alone should not deter further investigation both clinical and experimental.

Ochsner, Alton and Herrmann, George R.: Experimental Surgical Relief of Experimentally Produced Pericardial Adhesions. Arch. of Surg. 18: 365, 1929.

The authors have studied in 65 dogs the question of the removal of pericardial adhesions after the subsidence of the acute symptoms of acute pericarditis produced experimentally. In one group of animals a digestant was introduced in order to prevent the reformation of adhesions after the second operation. In another group of control animals physiologic sodium chloride was introduced into the pericardial cavity. In the third group merely the division of the adhesions was performed. In these groups with or without the introduction of saline solution, adhesions invariably reformed.

In three of the ten dogs treated by digital separation of the adhesions with the introduction of a digestant solution into the pericardial cavity no adhesions reformed. The remaining seven animals showed evidence of extensive pleural infection.

As the result of the study on these animals, the authors conclude that intrapericardial as well as extrapericardial adhesions are significant and produce cardiac embarrassment. The two types of adhesions are usually associated. They discuss the value of surgical intervention during the acute stage of purulent pericarditis in order to establish external drainage. They believe that further perfection of technic will enable them to introduce a vegetable digestant (not described in this article) into the pericardial cavity in order to prevent the reformation of adhesions following an operation devised to break these adhesions up.

Lockwood, Ambrose L.: Surgery of the Pericardium and Heart. Arch. of Surg. 18: 417, 1929.

In this article the author reviews the literature relating to this subject and discusses the various surgical procedures that have been devised to relieve injuries and disease of the heart. Among the important points to be learned from such a

study, the following may be mentioned. If the patient has lost much blood with a lowered arterial tension, the wound in the heart may temporarily cease to bleed, whereas when the patient's condition improves and the blood pressure rises delayed primary hemorrhage may occur and the patient may be found "in extremis." Injury of the bundle of His is often fatal. Pressure on the bundle of His or kinking and rotation of the heart by interfering with conduction through the bundle of His in doing the cardiorraphy may cause the heart to fibrillate or arrest entirely. Wounds of the heart heal by the formation of a cicatricial scar, not by true regeneration of muscle. Spontaneous eruption of the scar has frequently occurred following strain.

He also points out that a supporting stay suture through the apex is most valuable if elevation or rotation of the heart is necessary. Gauze should not be employed within the pericardium. Sterile water only should be employed to cleanse the pericardium. No antisepties should be employed to the serous surfaces.

Great care must be taken to avoid infection bearing constantly in mind that most of the deaths after twenty-four hours have been due to infection.

He concludes that cardiolysis in selected cases should be more commonly practiced. Cardiorrhaphy for injuries of the heart should be promptly undertaken when indicated, especially if hemorrhage is occurring.

Sutherland, G. A. and McMichael, John: The Pulse Rate and Range in Health and Disease During Childhood. Quart. Jour. Med. 22: 519, 1929.

The authors have noted that there is a normal variation in the heart rate of children between that of the sleeping and that of the waking hours amounting to more than thirty beats. This nocturnal slowing is probably of great importance for the child. Sleep for the child thus becomes a means of rest not only to the body but to the heart also. The authors believe that the explanation of the extreme variability of the pulse rate in childhood lies in the unstable nervous system of the child. They point out that the "normal" heart rate is present only when the child is asleep and when the unstable central nervous mechanism which controls the vagus and sympathetic nerves is free from disturbance of all outside stimuli. When the child goes to sleep, some time elapses before the effects of the stimulation of the nervous system during the waking hours pass off, the lowest level being reached between midnight and four A.M. They have also observed that when the child falls asleep in the early afternoon the pulse rate falls though usually not quite so low as the minimum nocturnal rate.

In studying a group of children with rheumatic carditis they have noted the pulse rate continues rapid day and night and cannot be slowed or altered by any amount of rest. This rapid pulse may be the only sign of activity in a case of rheumatic carditis. They feel that this is a useful sign to be noted in the care of children with carditis.

Derick, C. L. and Hitchcock, C. H.: An Address on the Allergic Conception of Rheumatic Fever. Canad. Med. Assoc. J. 20: 349, 1929.

In this address the authors review the literature and their own work on rheumatic fever which has brought about the conception that this disease may be of an allergic nature. They point out the similarity between this disease and tuberculosis and the development of hypersensitivity to tuberculous infection.

Much of the recent work done on streptococcus infections and on rheumatic fever in particular indicate the existence in certain individuals of a condition of hypersensitiveness to streptococci resulting from repeated low-grade infections or from the persistence of foci of infection in the body.

When under suitable circumstances, streptococci or products of streptococci are disseminated to the tissues, these tissues overact and the character picture of the disease results. When on the other hand there exists a condition of immunity or of normality in contradistinction to this peculiar hypersensitive state, the dissemination of streptococci results in a minimum of injury to the tissues and the characteristic phenomena of the disease fail to appear.

Kaiser, Albert D.: The Relation of the Tonsils to Acute Rheumatism During Childhood. Am. J. Dis. Child. **37**: 559, 1929.

In this survey 439 children who had acute rheumatism were studied and a special effort was made to determine the relationship of the rheumatic attacks to the presence or absence of the tonsils. Cases of chorea or rheumatic endocarditis were not included in the study unless there had been evidence of involvement of joints or muscles. Efforts have been made to answer the following questions in this study. Does acute rheumatism develop for the first time as frequently in children whose tonsils have been removed as in those not operated on? Nearly twice as many children in the community studied developed the first attack of rheumatism when the tonsils were still present. This marked difference in the incidence of the disease suggests that the presence of tonsils predisposes to the first attack of acute rheumatism and conversely that the removal of the tonsils offers considerable hope of escape from this infection. Two, Do recurrent attacks occur as often in children whose tonsils have been removed after one attack of rheumatism as when the tonsillectomy has not been performed? Recurrent attacks of rheumatism occur 10 per cent less often in children who had their tonsils removed after the first attack of rheumatism than in those whose tonsils were not removed. Three, Do recurrent attacks occur as often in children who have their first attack after the tonsils have been removed? The figures indicate that rheumatism developing for the first time in a child who has had the tonsils removed is more likely to recur than in the patient who is infected before tonsillectomy. Four, Does endocarditis occur as frequently in children who had acute rheumatism following a tonsillectomy as when the tonsils have not been removed? The incidence of carditis in the group of children studied is as high in one group who have had tonsillectomy as in those who have not.

Derick, C. L. and Swift, Homer F.: Reactions of Rabbits to Non-Hemolytic Streptococci. 1. General Tuberculin-Like Hypersensitiveness, Allergy, or Hyperergy Following the Secondary Reactions. J. Exper. Med. **44**: No. 4, 615, 1929.

In previous communications the authors have reported the phenomenon of secondary reaction to certain strains of green streptococci. Briefly this consists of an inflammatory reaction which appears about the 8th to 10th day after intracutaneous inoculation of rabbits with these microorganisms and at a time after the primary reaction has receded.

The object of this present communication is to present the detailed evidence which indicates that after the development of the secondary reaction animals have a type of hypersensitiveness which closely resembles so-called tuberculin allergy. This state is made evident by increased reactivity of the skin to reinoculation with small doses of these streptococci, by the marked reactivity of the scarified cornea to instillation of the streptococci into the conjunctival sac and by the death of many of the animals following intravenous inoculation with cultures in amounts well tolerated by normal rabbits. The lesions found in the lymphatic and hematopoietic organs of these animals are grossly very similar to those described originally by Koch in tuberculous animals following inoculations

with large doses of tuberculin. The authors have observed similar lesions in normal rabbits following intravenous injections of the more virulent hemolytic streptococci and have noted ophthalmic reactions similar to those seen in hypersensitive rabbits following primary inoculations of the cornea of normal rabbits with living hemolytic streptococci. Thus the condition of the hypersensitive rabbit has been altered in such a manner that the relatively avirulent nonhemolytic streptococci set up immediate reactions grossly comparable to those which follow infection of normal animals with virulent hemolytic streptococci.

The evidence brought out in this study shows that foci some place in the body are necessary for the development of this type of allergy because hypersensitiveness did not follow intravenous inoculation. Rapid destruction of the microorganisms without the production of large focal lesions probably offer a suitable explanation of this phenomenon.

The authors believe that following the intracutaneous inoculation of rabbits with any strain of streptococcus there develops a state of tuberculin-like hypersensitiveness but certain strains possess the capacity of stimulating the hypersensitiveness to a higher level than others and certain rabbits are more capable of reacting as is made evident by retesting the animals in different ways. Following the primary intradermal reaction there persists at this primary focus a certain amount of residual antigenic substance. When a sufficiently high degree of general hypersensitiveness develops, the cells in the immediate vicinity of the primary lesion are in a condition to react with small amounts of suitable bacterial substances whether they are either freshly introduced or residual. The secondary reaction is, therefore, apparently an evidence of this reaction with some residual antigen persisting at the site of primary inoculation in an animal which has developed a general state of hypersensitiveness. The peculiar feature is that some strains should possess these stimulating or reacting substances to such a degree, while others are strains apparently lacking in them.

Swift, Homer F. and Derick, C. L.: Reactions of Rabbits to Non-Hemolytic Streptococci. II. Skin Reactions in Intravenously Immunized Animals. J. Exper. Med. 44: No. 5, 883, 1929.

In previous papers it has been shown that rabbits inoculated in practically any manner except intravenously with sufficiently large doses of certain nonhemolytic streptococci develop a condition of tissue hypersensitiveness whereas if the primary inoculation of the animal had been by the intravenous route using amounts of culture and time intervals comparable with those employed in the hypersensitized rabbits these intravenously inoculated animals responded with none of these reactions of hypersensitiveness. The present paper presents evidence that these intravenously inoculated rabbits react differently than do normals or hypersensitive rabbits to intracutaneous inoculation.

These subsequent intracutaneous inoculations with homologous streptococci produce reactions with smaller and harder lesions than are shown by normal animals and they do not develop the general manifestations of hypersensitiveness such as are shown by animals previously inoculated into the tissues with the same cultures. The lesions have little or no edema and are hard and firm after 24 to 48 hours. These lesions show much less change in size after two hours than do the lesions in other types of animals. This reaction has been described by the authors as an immune type of reaction.

They also have noted that certain rabbits give reactions following intracutaneous inoculation which are soft, have very little color, fade rapidly and do not show secondary reactions. They occur in rabbits which appear sick either due to an overwhelming reaction from streptococci or from any other cause. They have

designated these reactions as cachectic and are seen in animals with a negative state of anergy. This type of reaction is in contrast to the hypersensitive animals who react secondarily with signs of redness and swelling. This type of reaction indicates a positive state of hyperergy.

Birkhaug, Konrad E.: Rheumatic Fever. J. Infect. Dis. 44: 363, 1929.

A series of 3,114 skin tests was performed during the summer of 1928 in European clinics on 594 individuals among whom were 42 active and 146 inactive or cured cases of rheumatic fever, carditis and chorea, 69 cases of chronic arthritis and degenerative arthritis and 33 per cent nonrheumatic controls. Excessive universal hypersensitiveness was found among 68 per cent of all types of acute rheumatic fever infection, to the filtrates or autolysates and bacterial suspensions produced by the hemolytic streptococcus.

Hypersensitiveness to nonhemolytic streptococcal products is most marked among active cases of rheumatic infection. Only 33 per cent of active and 29 per cent of inactive rheumatic fever individuals react to hemolytic streptococcal products, while 25 per cent of nonrheumatic controls react to the hemolytic and 14 per cent to the nonhemolytic streptococcal products. Among a series of 69 cases of chronic arthritis, 53 were due to infectious processes and 47 per cent of these react markedly to the products of both nonhemolytic and hemolytic streptococci.

Nye, Robert N. and Seegal, David: Non-Hemolytic Streptococci and Acute Rheumatic Fever. J. Exper. Med. 44: No. 4, 539, 1929.

Blood cultures have been taken from 25 available cases of acute rheumatic fever according to the methods of Clawson, Small and Birkhaug. These cultures were negative for nonhemolytic streptococci of both the alpha and gamma types. Nonhemolytic streptococci were frequently recovered from the throats of patients with this disease as well as from the throats of normal individuals.

Although these nonhemolytic streptococci were morphologically and culturally identical not only amongst themselves but also when compared with stock Small and Birkhaug strains, all including the latter have failed to show any noteworthy degree of homogeneity.

Representative strains of these streptococci have proved to be relatively nonpathogenic for rabbits following intravenous injection.

Hanzlik, P. J.: A New Method of Estimating the Potency of Digitalis: Pigeon-Emesis. J. Pharm. and Exper. Therapeu. 35: 363, 1929.

The author proposes a method for estimating the potency of digitalis directed toward the evaluation of a probable therapeutic dosage by determining the maximum emetic dose in pigeons.

Adult pigeons of from 300 to 400 grams body weight are used. The estimated dose of the digitalis preparation is injected into a suitable wing vein in the axillary region of the bird. On completion of the injection the pigeon is replaced into a cage for observation of vomiting which is recognized by downward craning movements of the head and usually flapping of the wings with occasional expulsion of gravel. These symptoms are generally preceded by symptoms of nausea, that is, swallowing due to increased salivation. lacrimation and ruffling of feathers of the head and neck. Vomiting occurs in from three to ten minutes depending on the dosage of the preparation used. In determining the minimum emetic dose a series of pigeons is injected and the just effective dose causing emesis in two out of three pigeons is noted.

The method has been compared with the official frog method and the cat method and a number of factors effecting the accuracy and application of the pigeon method have been considered. The method is simple, easy, convenient, economical and reasonably accurate. The minimum emetic dose of digitalis causes changes in the pigeon heart which are characteristic of advanced digitalis action thus further justifying expectations of therapeutic action when this dose per kg. in pigeons is transferred directly and given by mouth to man.

Hanzlik, P. J., and Stockton, A. B.: Results with the Pigeon-Emesis Method of Estimating the Probable Therapeutic Dose of Digitalis. J. Pharm. and Exper. Therap. 35: 393, 1929.

The circulatory and side actions of tinctures of digitalis, assayed by the pigeon-emesis method were observed in six convalescent and two pathological human subjects who received the preparations by mouth. The effects were controlled in three subjects receiving alcohol and atropine.

Fully developed actions of digitalis were produced in the majority of the subjects as indicated by sustained slowing of the pulse, fall of blood pressure and reduced pulse pressure, the doses agreeing closely with the probable doses estimated from the minimum emetic doses in pigeons.

Nausea and emesis occurred in one-half the subjects receiving the digitalis thus corroborating the high efficiency of the clinical dosage estimated from the minimum emetic dose in pigeons.

Conditions affecting the efficiency of the probable therapeutic dosage of digitalis in pathological conditions in circulation are discussed. Such dosage ascertained with pigeons and given in several divided doses orally, gave complete therapeutic responses in three out of four patients. Thus, the evidence taken together indicates that the pigeon-emesis method of estimating the potency of digitalis appears to predict the probable therapeutic dose for man.

Burwell, C. Sidney, and Smith, W. Carter: The Output of the Heart in Patients with Abnormal Blood Pressures. J. of Clin. Invest. 7: 1, 1929.

In two groups of cases one with systolic blood pressure of over 175 mm. of mercury and one with systolic blood pressure of less than 95 mm. of mercury the total cardiac output per minute per kg. of body weight and the cardiac output per 100 c.c. of oxygen absorbed did not show significant changes.

The cardiac output of all the subjects in both groups falls within the limit seen in normal healthy people. When the blood pressure is within the usual zone the averages of the cardiac output in the two groups are almost identical. The absence of variation is striking when it is observed that the average pulse pressure in the hypertensive group is 85 mm. as against 26 in the hypotensive group.

The basal metabolic rate is on the whole somewhat higher in the group with high pressures than in the group with low. The pulse rates in both groups with the exception of those of the two normal men are slightly above the low level usually attained under satisfactory basal conditions and the average rate is higher in the hypertensive just as is the metabolic rate.

These observations demonstrate that under conditions of bodily rest patients with arterial hypertension have no significant increase in the cardiac output.

Esler, James W., and White, Paul D.: Clinical Significance of Premature Beats. Arch. Int. Med. 43: 606, 1929.

The present study consists of a series of 200 patients, 100 of whom showed premature beats and 100 normal rhythm. None of them evidenced a marked degree of auriculo-ventricular or intraventricular block. They were seen between

the years 1915 and 1926, have been studied by electrocardiograms and have been followed to the present time. The clinical diagnoses in the cases of the two groups were similar.

Premature beats which occurred at the more rapid rates in this series did not bear a more serious prognosis than those at slower rates, when allowance was made for the increase in mortality due to increased rate alone. The presence of premature beats in the series reported here added no gravity to the prognosis. The death rate was actually slightly greater in the 100 cases with normal rhythm.

Auricular premature beats and multifocal ventricular premature beats did not appear to bear a much more serious prognosis than the usual unifocal ventricular premature beat.

The authors conclude that the frequency with which premature beats occur in a given case seem to bear little relation to prognosis.

Stewart, Harold J.: A Study of Certain Effects Occasioned in Dogs by Diphtheria Toxin. Arch. Path. 7: 767, 1929.

Following the intravenous injection into dogs of diphtheria toxin it was noted that most of these dogs showed progressive decrease in the amplitude of the R_2 and R_3 waves of the electrocardiogram. The present paper analyzes these changes in the apparent size of the heart. The analysis of the factors involved in this alteration indicates that it is due to loss of weight by the heart, although other factors possibly play a part. The author has studied the change in body weight, the number of red blood cells and the amount of hemoglobin. There was also no consistent change in the total blood volume. Histological study of the muscles of the heart did not reveal an actual destruction of the cells to account for the decrease in weight.

Otto, Harold L.: The Ventricular Electrocardiogram. Arch. Int. Med. 43: 335, 1929.

The author has studied the nature of disturbances in the component portions of the ventricular electrocardiogram by using various preparations that would either destroy or irritate the heart muscle. In 48 experiments on dogs the heart muscle was destroyed by injections of 95 per cent solution of alcohol. Various regions of the heart were injected.

Extensive destruction of the heart muscle can be made in this way before it causes circulatory failure. The injection of an irritant like hypertonic saline solution does not significantly alter the electrocardiogram. The electrocardiographic changes which occur from injections of alcohol are due to the destruction of the muscle, irritation of the muscle playing no part.

The author has also noted that mechanical irritation of the ventricular muscle was without effect on the electrocardiogram and also that the amount of injection which was usually necessary to affect the T wave permanently was considerably less than that required to affect the QRS. Contrasted to the T wave, this portion of the electrocardiogram was stable and did not give indication of the changes which had taken place within the myocardium.

Weiss, Soma and Blumgart, Herrmann L.: The Effect of the Digitalis Bodies on the Velocity of Blood Flow Through the Lungs and on Other Aspects of the Circulation. A Study of Normal Subjects and Patients with Cardio-Vascular Disease. Jour. Clin. Invest. 7: 11, 1929.

Strophanthin and tincture of digitalis were administered intravenously and by mouth respectively to eight normal persons. Their effect on the velocity of pul-

monary and peripheral venous blood flow, on the vital capacities of the lungs and arterial and venous pressures was observed. Amounts of these drugs corresponding to large therapeutic doses failed to change appreciably the velocity of the pulmonary blood flow and the above-mentioned aspects of the circulation in the normal subjects.

When strophanthin or tincture of digitalis in large therapeutic doses was administered to 14 patients suffering from cardiovascular disease, the velocity of the pulmonary blood flow became increased in seven, was unaltered in four, while in three patients it was definitely decreased.

Although the average pulse rate in seven patients showed a reduction of 14 beats per minute, the pulmonary circulation time showed an average reduction of 6.9 seconds which corresponds to an increase of 30 per cent in the velocity of pulmonary blood flow.

The velocity of blood flow in the pulmonary circuit is decreased in patients with circulatory failure. With clinical signs of improvement due to the administration of digitalis or to rest the velocity of this blood flow increases although the degree of the patient's improvement and the change in velocity may not be parallel.

Wolff, Louis and White, Paul D.: Auricular Fibrillation. Results of Seven Years Experience with Quinidine Sulphate Therapy. Arch. Int. Med. 43: 653, 1929.

In 1923 Viko, Marvin and White reported 71 cases of nonparoxysmal auricular fibrillation and 4 cases of auricular flutter. In 68 per cent of these patients the rhythm was restored to normal by quinidine but in only 34 per cent was it maintained during the period of observation, which varied from a few days to more than 10 months. The data obtained from the follow-up study of these patients is presented in this present article.

The second group consists of patients seen since the first report was made and therefore is composed of new patients. The total number of 70 cases comprises 62 of fibrillation and 8 of flutter. Of this entire group circus movement was abolished in 36 or 65.7 per cent.

In apparently normal hearts consisting of 7 cases in this series, premature auricular fibrillation was terminated by quinidine in 100 per cent of the cases, irrespective of the age of the patient and the duration of the fibrillation. These patients are the most satisfactory to treat. The next most responsive group is that of patients with rheumatic heart disease who are less than 41 years of age. In the hyperthyroid group the response is somewhat better than in the group of patients with hypertensive and arteriosclerotic heart disease.

When not dealing with normal hearts the most important single factor which influences the outcome of the treatment is the duration of fibrillation. This is true in a limited sense only, for the response is surprisingly high when the fibrillation has lasted less than a month. Beyond this, duration apparently is of little or no importance. Age is important in the group of patients with rheumatic heart disease. The desired response occurs in a high percentage of the young patients, but occurs in a much smaller proportion of the patients more than 40 years old. Etiology has but a minor influence on the response to quinidine therapy.

Recent congestive failure reduces the probability of success from the use of quinidine. The duration of fibrillation has not accounted for the poor response in the cases with congestive failure. A past history of congestive failure, the size of the heart when enlarged, the type of fibrillation and sex appears to be of no influence on the outcome of treatment.

Factors contributing to failure in some of the cases in this series were insufficient quinidine doses, intercurrent infections and possibly alcoholism. In this

new group of 70 patients there was one death which might possibly be attributed to quinidine but probably was not due to it. The history of fibrillation for a great many years in the absence of valvular disease and congestive failure, recent or present, is not a contraindication for quinidine therapy.

It seems highly desirable to digitalize all patients as a matter of routine before starting quinidine. Full therapeutic doses should be used. There is clinical, experimental and theoretical justification for this view. Digitalization is not indispensable in many cases but in some it will spell the difference between failure and success. Often normal rhythm may be attained with smaller doses of quinidine if digitalization has been resorted to. It may add to the comfort of the patient, improve his condition and possibly prevent fixed flutter. No harm has been observed from the combined use of digitalis and quinidine.

Quinidine is of value in preventing and terminating paroxysmal auricular fibrillation and is effective in some cases of paroxysmal tachycardia and premature beats. In cases of auricular flutter digitalis is probably more effective than quinidine. Digitalis appears to be more effective than quinidine in occasional cases of paroxysmal auricular fibrillation and paroxysmal tachycardia. In judging the value of quinidine in premature auricular fibrillation the criterion of greatest importance is the permanence of the results obtained. These follow-up studies have indicated that restored normal rhythm is permanent in a significant number of patients and although there is no definite evidence that normal rhythm prolongs life or reduces mortality, it is clearly evident that it promotes the health of the patient.

Harris, Kenneth E.: A Series of Cases of Auricular Fibrillation Treated with Quinidine Sulphate with Special Reference to the Duration of the Restored Normal Mechanism. Heart, 14: 283, 1929.

Forty-three consecutive cases of auricular fibrillation were treated with quinidine sulphate during the period of 1921 and 1923. The immediate results, together with the after histories of those patients in whom normal rhythm was restored are now recorded. In 26 of the 43 cases (60.5 per cent) normal rhythm was restored. The 26 patients who reacted successfully have been kept under close observation for the purpose of ascertaining how long the heart rhythm would remain normal. At the end of the first month auricular fibrillation had reappeared in 9 cases, while in 17 normal rhythm persisted. By the end of 6 months fibrillation had reappeared in 2 more cases. At the end of one year fibrillation had reappeared in 16 of the original series. During the next year three more reverted so that at the end of two years 6 cases were known still to present normal rhythm. Of these 6 patients 4 resumed the condition of fibrillation after periods over two, three and one-fourth, four and one-half and seven years respectively. One has not been heard of since July, 1926, the other is still normal for four years. The two patients that have been untraced, presented normal rhythms for 317 and 1673 days after quinidine therapy.

Wolff, Louis and White, Paul D.: Auricular Standstill During Quinidine Sulphate Therapy. Heart, 14: 294, 1929.

The two cases reported in the present communication furnish evidence that temporary auricular standstill may occur when auricular fibrillation ceases under the influence of quinidine. The effect of quinidine in this connection may be due to its poisonous action to the auricular muscle. There is experimental evidence that quinidine depresses the sino-auricular node and that it may induce intra-auricular block and auricular standstill.

Levine, Samuel A. and Fulton, Marshall N.: The Effect of Quinidine Sulphate on Ventricular Tachycardia. J. A. M. A. 92: 1163, 1929.

Clinical experiments in ten cases showing paroxysmal or persistant tachycardia of ventricular origin indicates that quinidine sulphate has in most instances a specific effect on restoring a normal rhythm.

Ventricular tachycardia occurs occasionally in patients who have no organic heart disease but more commonly in those with coronary thrombosis. Although quinidine does not have any effect on the other complications of coronary thrombosis such as rupture of the heart or production of emboli, its beneficial influence on ventricular tachycardia is most dramatic and may be life saving.

It is highly probable that ventricular tachycardia is of the nature of a circus movement like that of auricular flutter and auricular fibrillation and that the effect of quinidine is similar in all these conditions.

Moore, Henry: Paroxysmal Ventricular Tachycardia. Irish J. Med. Sci., 754, Dec., 1928.

A case of paroxysmal tachycardia in a boy 12 years old, probably arising in the ventricular muscle is described. The patient has been under observation for more than 56 months. The attacks have become less frequent and of shorter duration. Electrocardiograms are presented showing the character of the waves during the attacks and intervals of regular sinus rhythm. The attacks occurred spontaneously, were readily induced by the administration of atropine and whether spontaneous or induced by atropine were readily terminated by giving quinidine orally. They usually started with an abrupt change in the form of the QRS complex and approximately a normal heart rate. The ventricular rate during the attack rose to about 170 per minute. The T wave in the slow atropine paroxysm was upright whenever recorded, whereas it was inverted in the slow spontaneous attacks.

Coombs, Carey F.: The Distal Phenomena that Accompany High Arterial Tension. Bristol Medico-Chirurgical J. 46: 35, 1929.

In this address the author described the effects to be noted in the body as a result of high arterial tension. He mentions the effect in the cerebral circulation and the brain, in the peripheral muscles and other tissues. He believes that all of these phenomena can be ascribed at least in part to gradual wearing down of the elasticity of the arterial tree. He believes that the importance of obstruction in the small vessels is not substantiated by examination of the tissues.

Hare, D. C. and Karn, M. Noel: An Investigation of Blood Pressure, Pulse Rate and the Response to Exercise During Normal Pregnancy, and Some Observations after Confinement. Quart. J. Med. 22: 381, 1929.

The object of this investigation has been to study the physiological reactions of the circulation during the course of normal pregnancy. The methods employed were blood pressure and pulse rate measurements and the response of the pulse rate to an exercise test. One hundred and six individuals are included in the study, three-fourths of whom were seen several times at intervals of four weeks or more. A suitable group of nonpregnant women were examined as controls using the same methods under the same conditions.

It was found that the average systolic blood pressure of healthy women during pregnancy is lower than the average of nonpregnant women; also the average deviation during pregnancy is less and the range is consequently slightly smaller.

Changes during the course of pregnancy show a tendency to a lower pressure in the middle period than in the earlier weeks and there is a slight but significant rise in the last three months. Any considerable rise is to be associated with the onset of a toxic condition. The mean diastolic pressure during pregnancy is not significantly different from that of nonpregnant women. During the first six months the mean pressure is below the general mean and there is a steady rise from the seventh month to a maximum in the last month which is higher than the mean for nonpregnant women. The pulse pressure is lower than that of nonpregnant women and falls with the advance of pregnancy.

Pulse rate during pregnancy is not significantly altered from the normal. The difference between the sitting and standing rates is within the range of the normal increase. The pulse rates show no significant correlation with the period of pregnancy.

An exercise test is well performed and the pulse rates after exercise are not significantly different from those of controls. In the last months of pregnancy the mean rates after exercise are below those of the preceding periods. The rates after exercise are highly correlated with the resting rate.

There is no evidence to be found in this work of embarrassment of circulation during the later months of pregnancy.

Harris, Kenneth E.: Notes on a Case of Complete Heart Block of Unusually Long Duration. Heart, **14:** 289, 1929.

Complete heart block in a healthy and active man with case notes over the remarkably long period of 28 years is here recorded. The earliest notes are from the hospital records in 1900 and the first graphic records are those taken in 1909. The patient now 50 years of age, is still vigorous and in no way incapacitated.

The first manifestations of heart block were the short signs of serious syncopal attacks. The case is unusual not only for its duration but especially because the man has enjoyed vigorous health without limitation of his capacity for physical work throughout the whole period named.

Redisch, W., and Rosler, H.: Contributions to the Knowledge of Congenital Heart Lesions. V. Capillary Studies. Wien. Arch. f. inner. Med. **16:** Part 2/3, 463, 1929.

In 36 cases of congenital heart disease, four of which have been controlled by autopsy and in 10 cases of acquired heart disease the picture of the capillaries has been studied. In morbus caeruleus there is an extreme capillary hyperemia with special involvement of the various parts of the capillaries, stasis and new formation of capillaries. With Pacchioni, the authors consider this congenital capillary dilatation as the chief cause of the extreme cyanosis, typical of severe congenital heart disease.

In two cases of stenosis of the isthmus of the aorta they have found numerous capillary aneurysms and small and thin capillaries of the toes in contradistinction to the well developed capillaries of the upper extremity. Cases with defect of the septum and open ductus Botalli showed a normal capillary picture. No connection was found between the clubbing and the capillary changes.

Nicholson, Gertrude and Shulman, Harold I. and Green, Dorothy L.: Congenital Heart Block with Report of a Case. Am. J. Dis. Child. **37:** 280, 1929.

An instance of congenital cardiac defect with peculiarities of pulse rate and rhythm is presented. The electrocardiogram shows the arrhythmia to be due to

a defect in cardiac mechanism which varies in its action. In this type of lesion of the heart, high grades of heart block are seen frequently to alternate with complete dissociation. The theory that this change is due to variance in tissue tension around the defective conducting fibers is suggested.

Aalsmeer, W. C. and Wenckebach, K. F.: The Heart and Circulatory System in Beri-Beri. Monograph, Urban and Schwarzenberg, 1929.

Beri-beri not only produces degeneration of the nerves and hydrops but is responsible for important cardiac symptoms. These so far have been explained by degeneration of the vagus nerve. Aalsmeer who studied the diseases in Java describes three forms. (1) A mild form occurring in ambulatory patients. Dyspnea and palpitation may be present in these cases and on examination the precordial pulsation is wave-like, the heart sounds are very loud and although no change in the heart size is usually made out on examination, the fluoroscope will reveal an increase in the size of the right heart. Rest and administration of vitamine B offers an effective therapy. (2) A moderately severe type. This occurs in the patients who already show edema and polyneuritis although cardiac symptoms may be absent in such cases, most of the patients complain of a feeling of pressure in the heart region, relieved on lying down. Cough, dyspnea and cyanosis are not usually present. Again the waving pulsation in the precordium is present, the heart is enlarged to right and left and a systolic murmur can be heard over the left heart. Hydrothorax may be present and is usually a part of the general edema rather than of cardiac origin. The spleen and liver are enlarged and tender. (3) An acute pernicious form of beri-beri. The chief symptoms are precordial distress localized to the sternum (Shôshin) accompanied by extreme dyspnea. The physical findings are as in the previous type excepting that the right heart is relatively much increased in size. No edema of the lungs is present, the onset is sudden and the course fatal. Intra-cardiac adrenalin is occasionally of benefit. Venesection is useful and relieves the feeling of oppression and precordial pain.

A chronic form of cardiac beri-beri has been described. This probably occurs in patients who have had the acute form of the disease and who have reverted to their deficient diet.

The blood pressure in beri-beri shows no change. The roentgenogram shows right-sided enlargement of the heart; signs of congestion of the lungs are rarely visible. The electrocardiogram shows a shortening of the conduction time with tachycardia. The P-R interval may be 0.12 second or shorter. Pathologically both right and left ventricles are dilated with increase in the size of the muscle especially on the right side. The heart muscle itself seems unchanged.

The precordium usually contains between 10 and 200 c.c. of fluid. Lung congestion is not usually present but emphysema may be found. The treatment consists of rest in bed, corrected diet and venesection. Strychnin may be used, digitalis and strophanthin are without effect. The heart symptoms are due to failure of the right heart, but it is improbable that emphysema of the lungs, changes in the pulmonary artery or degeneration of the vagus nerve could be responsible for this condition. Wenckebach believes that when the whole heart becomes weaker the right heart will fail first and this failure will be the cause of death. This probably occurs in other forms of heart disease but not in such a clearly cut manner as in beri-beri, since other types of heart disease are usually accompanied by valvular defects, fibrillation, etc. It has been shown that in the frog heart swelling of the muscle will produce some failure of contraction although the stimulus will be conducted normally, thus a similar phenomenon in beri-beri would account for the decreased cardiac activity with the more rapid conduction

time. The vitamine deficiency may act by changing the colloidal water binding capacity in certain predisposed tissues. Reversibility of this process would support this theory. Administration of the B vitamine has the same specific effect in beri-beri as thyroid has in myxedema.

Kurtz, Chester M. and White, Paul D.: The Treatment of Subacute Bacterial Endocarditis by Transfusion from Immunized Donors. New Eng. J. Med. 200: 479, 1929.

In a slowly progressing case of subacute bacterial endocarditis, immunized transfusions from donors vaccinated with a killed culture obtained from the patient's blood were tried. One massive transfusion of 1800 c.c. and five smaller ones (500 c.c. each) were given without any appreciable effect on the course of the disease which terminated fatally seventeen months after the onset. Serological studies showed the antibody titer to be higher in the patient than in any of the donors. The authors believe that this case indicates that patients with this infection have an opportunity to develop a certain amount of active immunity because the Streptococcus viridans is of rather low virulence and the disease progresses slowly. It is probable that the immunity is greater than can be induced by vaccinating a healthy donor.

Book Reviews

Clinical Electrocardiograms, Their Interpretation and Significance. By Fredrick A. Willius, M.D. Section on Cardiology, The Mayo Clinic, Rochester, Minnesota, and Associate Professor of Medicine, The Mayo Foundation, University of Minnesota. W. B. Saunders Company, 1929, Philadelphia, pp. 219.

This volume, one of the Mayo Clinic monographs, is, as its title indicates, a clinical guide to the reading and interpretation of electrocardiograms. The book is carefully planned, omitting all discussion of method, technic and theory, but considering in order the normal electrocardiogram and the various deviations from this: ventricular preponderance, the arrhythmias, individual wave changes, dextrocardia, coronary thrombosis, and records obtained from the dying heart. The text is clear and concise, written in condensed direct style, and valuable because of the author's wide experience. The chief value of the book, however, lies in its illustrations. The 368 figures have been selected with care to show not only typical tracings but also transitional changes and combinations of several abnormalities. The figures are clear cut and are accompanied by unusually full legends. The tracings and legends comprise a fairly complete text and reference book, but for those who wish to pursue more detailed study there is a good bibliography with references arranged at the end of each chapter. An adequate index enhances the value of the text. This book should be of value to all who are interested in the interpretation and significance of electrocardiograms.

Diseases of the Heart and Vessels. By Ernst Edens. With 239 partially colored pictures. 1057 pages. Berlin. Julius Springer, 1929.

As the author says in the introduction, this book intends to give a critical review of our present knowledge of the diseases of the heart and vessels and the appropriate therapy. After an abstract of the historical development, the anatomy and physiology of the circulatory system are given. The methods for the examination of the circulatory system are described. Following this then is a study of the valvular diseases with their consequences and cardiac insufficiency. A special chapter is devoted to the functional test of the heart and the vessels. A great space is occupied by the therapy of cardiac insufficiency which covers all the problems of modern treatment of heart patients. The physical methods of treatment are given the consideration which they deserve. The next chapter contains the description of valvular lesions with their clinical and therapeutic peculiarities. Next follow the malformations of the heart and the diseases of the heart muscle. The mutual relationship between the heart and factors which make up body constitution is discussed. A special chapter is devoted to the study of mechanical conditions under which the heart is working and its changes under pathological conditions. A thorough chapter on the irregular activity of the heart and its treatment closes the part of the book dealing with the heart alone. A chapter follows on the diseases of the pericardium.

The diseases of the vessels are separated in three divisions: those of the arteries, the veins and the capillaries. An especially broad discussion on angina pectoris and a short review of the neurosis of the heart and vessels finish this part of the book. The text is accompanied by excellent pictures, curves, tables and electrocardiograms. The print is good. An index with the authors' names and the subjects and an extremely comprehensive accumulation of the literature (246 pages) complete the book and make it a very valuable addition to the well-known textbooks of heart disease for the student, the practitioner and the research worker.

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Original Communications

SOME UNSOLVED PROBLEMS CONNECTED WITH ACUTE OBSTRUCTION OF THE CORONARY ARTERY*

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The purpose of this paper is to present in outline certain features of acute occlusion of the coronary artery concerning which there is still some obscurity. The hope is that a frank statement of these problems may stimulate clinicians, pathologists, and experimental workers to study and solve them. It is to be noted that acute occlusion of the artery is the only topic under consideration. Chronic, i.e., slowly progressive occlusion is not sharply demarcated from the acute process, but its features are of somewhat different character and may well be separately considered, at least for the present.

RELATION TO INFECTION

Occasionally the occlusion is by an embolus. Generally, however, a thrombus is the cause. In practically all the thrombotic cases in which autopsy has been performed a chronic change in the vessel wall is mentioned—atheromatosis, especially patchy atheromatosis; roughening; calcareous plaques; narrowing, especially at a point of bifurcation; arteriosclerosis. That this chronic change is the sole cause is not clear.

What may be the influence of physical or chemical changes in the blood, or of an altered number of blood platelets is unsettled. Does a slower or feebler blood current have any effect? Particularly, what is the influence of infection? Several writers have called attention to the frequency with which acute coronary occlusion has been preceded by general infectious processes or by a local infection in another part of the body. They suggest a secondary inflammation of the wall of the coronary artery as a factor that may favor thrombosis. In connection with rheumatism and other infections acute changes in the walls of arteries have been noted. It is suggestive as fitting in with clinical experience that von Glahn and Pappenheimer find that the arteritis due to pyogenic infections may cause thrombosis while that

*Read at the Meeting of the Association of American Physicians, Atlantic City, May 7, 1929

accompanying rheumatism seems not to show this tendency. Boyd's studies are worthy of note. He shows acute mural changes in the coronary artery in addition to the chronic, and believes there is definite evidence of an inflammatory basis for coronary occlusion.

Here, then, is a problem: to discover what factors aside from the chronic change in the vessel wall determine the formation of a thrombus; especially, to what extent do focal or general infections play a part in this process? In what proportion of cases does the wall of the coronary artery show acute as well as chronic changes that might favor thrombotic occlusion? Do certain infections favor thrombosis while others do not? Why is it that syphilis that so often works damage to the aorta and the mouths of the coronaries plays such a minor part in the tragedy of acute coronary occlusion?

EMBOLIC PHENOMENA

Secondary embolic manifestations may occur soon or late after myocardial infarction. Some report this as a not uncommon complication. Others have seen comparatively few instances. The explanation offered for the occurrence is that from the intracardiac thrombus that so commonly forms over the infarcted area fragments are detached that, as emboli, obstruct peripheral vessels. There are clinical and post-mortem reports of coronary occlusion with emboli in the arteries of the brain, spleen, mesentery, retina, and extremities. If the intracardiac thrombus is in the right heart the emboli may produce pulmonary infarction.

Granting that the origin of the emboli in the intracardiac thrombus is the probable explanation, the question may yet be raised whether there may not be another origin, at least in some instances. If an infectious process has produced coronary arteritis may not this same process produce as well a similar change in the wall of some other artery, e.g., in the brain, leg, or spleen? The weak action of the heart and the feebler blood current, results of the damage done to the myocardium, may still further favor thrombus formation.

The question then seems proper: May the supposed secondary embolic manifestations at times be due to multiple thrombi resulting from widespread acute arterial inflammation?

In this connection it may be recalled that some regard postoperative pulmonary infarction as often due to the formation of a thrombus in situ rather than to an embolus having its origin in a thrombosed vein at the seat of operation.

PHLEBITIS

There are few observations on the condition of the coronary veins in cases of this accident. Is there evidence of phlebitis or of venous thrombosis? If such changes are present, what is the effect on the heart's activity? What is the state of the thebesian vessels?

CAUSE AND MANNER OF DEATH

Many patients die soon after the artery is obstructed, in a second or in a few minutes. Is this a sudden stopping of the heart's action or is there a fibrillation of the ventricle that precedes death? When patients die suddenly as they often do, hours or days after the accident, is this due to suddenly developing fibrillation of the ventricle? Probably, yes, but it is not proved. How often is death due to rupture of the heart? How often to gradual heart failure with its ordinary symptoms—dyspnea, râles, cyanosis, edema, albuminuria? In how many cases is death due to a new thrombus that forms in some other artery of the heart? Is this, as Sternberg suggests, especially apt to occur in an artery at the edge of the infarct? Or is death often due to the increase of the original thrombus proximally, thus enlarging the area of infarcted and useless muscle?

INFLUENCE OF COMPENSATORY ENLARGEMENT OF ANASTOMOSING VESSELS

Paradoxical as it may sound, the heart whose vessels are extensively sclerosed may often better withstand the insult of sudden coronary occlusion than the one whose vessels are comparatively normal. If one of the coronaries is the seat of sclerosis that increases with advancing years, there may be a compensatory enlargement of the collateral and anastomosing branches. This feature with the description of the intricate capillary anastomosis is stressed by Oberhelman and LeCount in their article of 1924. The importance of the thebesian vessels in keeping alive a heart whose coronaries are extensively obstructed has been shown by Wearn, Scott and others.

It is only by recognizing the extensive intercommunication of blood vessels in the heart and the mutual dependence of one artery on the other that one can understand the ability of the heart to stand up under the shock of sudden occlusion of a large branch, a main trunk of a coronary, even the plugging of both coronaries, as in cases cited by Wearn and by Scott.

This question is worthy of still further study. Is there any way of deciding clinically by symptoms, by x-ray or electrocardiograph, what may be the prognosis? This depends largely, we may assume, on the condition of the intact portion of the heart muscle as well as on the capacity of the infarcted area to heal by scarring, and both these processes depend largely on the efficiency of the collateral circulation.

LOCALIZATION OF THE INFARCT

The immediate and remote effects of the accident will depend, not alone on the suddenness and completeness of the occlusion, but in large measure on the size and location of the artery involved, whether right or left coronary, descending or circumflex branch, small laterals, etc. Is it possible by symptoms, physical signs or instrumental aid to state the vessel occluded and the area of heart muscle secondarily damaged,

and thus gain knowledge that may be helpful in estimating the outcome or that may serve as a guide to treatment? Can we, in other words, localize the lesion as we do when a cerebral artery is occluded?

There is a difficulty in this problem that is inherent in the fact that the area of myocardial softening will depend much on the degree to which anastomoses are present and as already stated the degree to which compensatory changes have taken place in collateral vessels. In one heart the results of an occlusion near the origin of the descending branch of the left coronary artery may differ materially from a similar obstruction at the same place in another.

The electrocardiograph should here be extremely helpful. The fruitful experimental and clinical work of Fred Smith, Pardee, Parkinson and Bedford, and others is well known. But further animal investigation is desirable. Of greater value, however, will be the careful correlation of electrocardiographic study in man with check by postmortem findings. More accurate knowledge must surely come from such investigation.

It is probable, too, that we are not as painstaking in our examination of these patients as we should be. It would seem as though variations in the intensity and quality of pain and its radiation, in skin tenderness, dyspnea and cyanosis, drop in blood pressure, nausea, and vomiting, might all be significant, if properly analyzed, in helping to decide where the obstruction and the myocardial lesion lie. As is known, attempts have been made by Pletnew and by Libman, to differentiate between a lesion in the right coronary and in the left. In the former engorgement of the liver, in the latter dyspnea, fall in blood pressure, and other signs of pulmonary congestion are regarded as cardinal differentiating points. These observations should be continued. In this connection it must not be forgotten that the infarction effect of an obstruction of the left coronary is not limited to the muscle of the left ventricle nor does an obstruction in the right coronary soften only the muscle of the right ventricle. Not only are the septum and certain papillary muscles generally involved but there is more or less lapping over of the effect into the other ventricular wall in either case. This is because, as is well known, the right coronary artery sends a branch that goes to the posterior wall of the left ventricle. The left coronary helps supply a portion of the anterior wall of the right ventricle. So, pure right and pure left ventricular softening are not so very common.

X-ray examination may show the cardiac contour altered by the yielding, weakened wall. Possibly percussion may help in the same way. The location of a pericardial friction might at times be interpreted as indicating the location of the myocardial lesion. The problem of localization is therefore a live one and there are several avenues of approach.

PERICARDITIS

In what proportion of cases is the pericardium at autopsy found to be roughened? In how many of these has friction been heard? If not heard, does the location of the pericardial lesion posteriorly or laterally rather than anteriorly explain the failure to hear the abnormal sound, or is such failure due to lack of keen examination, or may such lesion exist and be noiseless? How often is there an infarct that, extensive in the subendocardial region, fails to reach the pericardium? Are the cases with friction more severe in type and of more serious prognosis than those without?

MILD TYPES

How often do mild types of the accident occur? All grades of severity exist. There are forms with instant death or death in a few minutes or hours; or with death postponed for days or even months. There is the form with stormy onset, severe reaction and then a recovery as regards life but with residual damage to the heart slight or serious as the case may be. There are mild cases, mild as to onset, as to early symptoms and late effects. That these mild cases are of greater frequency than is generally recognized is almost certain. Some of these patients fail to consult the doctor because the upset seems of no moment. Or the pain and other disturbances seem negligible to the physician and he fails to note slighter symptoms that are really full of meaning—slight drop in blood pressure, transitory dyspnea, moderate tachycardia, a trifling rise in temperature, or a little increase in the leucocytes. That these milder cases with prompt recovery are really of the nature of coronary thrombosis is at times shown by the fact that later a clear-cut attack of severer form may occur, recognized by patient and doctor as of the same character as the earlier mild one, differing chiefly in degree. Autopsy often reveals not only the recent infarct but also one or more older healed lesions with the anciently obstructed vessel.

In what way may these cases be recognized more definitely? By what grouping of historical data, symptoms, signs, and instrumental findings may we be able to state that this accident has occurred? Just as I have finished this paragraph there comes to hand the meaty article by Harold J. Stewart in the AMERICAN HEART JOURNAL for April, 1929. He expresses this same idea more succintly and forcefully than I have when he says: "The minimum signs and symptoms upon which one may venture to make a diagnosis of coronary occlusion and to give and estimate the state of the coronary vessels and of the heart muscle are not known."

The problem then is what are the minimum signs and symptoms?

RECURRENCES

How often are recurrences encountered? Surely not infrequently. It is almost a tradition that a patient who has had one cerebral stroke—a large proportion of such accidents being thrombotic—is liable to have another. Similarly a myocardial ictus, to use the French term, may be repeated. Recently at autopsy a fresh thrombus and infarct were found together with an old extensive scar with thinning of the walls, aneurysmal bulging, and obliterated coronary. The history recorded that seven years before, the patient had suffered a severe, painful, heart attack that had confined him to bed for many days.

Recurrences generally occur at shorter intervals than seven years. What is the rule as to time, if there is any rule? Are the recurrences as in the case cited due to new thrombi in other vessels, or are they oftener due to a proximal enlargement of the old thrombus?

PAINLESS ATTACKS

Among the outstanding symptoms in most descriptions of acute coronary occlusion is pain. This is generally described as sudden, often unprovoked by effort, severe, unyielding to nitroglycerin, requiring morphine. It may be typically anginal as to substernal location, brachial radiation, vise-like or gripping character. Often, however, it is low in the sternal region or is referred to the epigastrium.

But there is no doubt that there are cases with mild pain or with no pain at all. While in my own experience pain has been present in nearly all of the cases I have regarded as acute coronary occlusion, it has at times been absent or it has not been the earliest or most striking feature. In one case, otherwise perfectly typical, a weakness and dizziness marked the onset; and even several hours later there was no pain requiring morphine, merely a precordial distress. This substitution of sudden dyspnea for pain was aptly referred to by Obrastow and Strachesko as a pain equivalent. Rapid drop in blood pressure may be added to dyspnea as another pain equivalent. To what extent and in what way then may we recognize acute coronary occlusion in the absence of pain?

It may be added that when Gallavardin and other French writers say that pain is of secondary importance and a relatively rare incident in the clinical picture attending coronary occlusion, they are not drawing the line between acute or sudden obstruction of the artery that is attempted to be drawn here. If the ingravescent and slowly developing cases are included, pain undoubtedly is relatively much rarer.

Also, are pain and other typical features, as Wearn and others have noted, more apt to be lacking when an artery is obstructed in an individual whose heart is already failing, perhaps through old valvular

disease or degenerative myocardial processes? Is coronary obstruction extremely rare in association with auricular fibrillation, or is its apparent rarity due to the fact that it is easily overlooked because the well-known striking symptoms are missing? Are masked and atypical forms not unusual under these conditions?

ANGINAL PAIN BEFORE AND AFTER ATTACKS

There are quite divergent statements regarding the cessation or persistence of anginal pain after an acute coronary occlusion. In some instances no anginal manifestations have preceded the attack, and after the subsidence of the initial suffering no painful residue is left; there is no pain even on exertion. In other cases the occlusion ushers in a status anginosus generally resulting fatally in a few hours or in a few days. Or there may develop when the acuter symptoms have gone, the features of ordinary effort angina. On the contrary there are many instances where in a sufferer from angina, perhaps with hypertension, the painful paroxysms on walking have disappeared after the date of infarction. Some regard this as the almost invariable rule. There would seem to be, however, no justification for such a generalization; there seems to be no uniform result of the accident as regards pain of anginal character.

Further observations are desirable along this line. Perhaps some explanation may be offered for the various types of pain left after the occlusion.

BEARING ON THE THEORY OF ANGINA PECTORIS

What bearing has acute occlusion on the theories of angina pectoris? Without attempting to answer the question or to advance arguments it would seem that the phenomena attending the sudden obstruction of a coronary artery tend to strengthen the view that the paroxysm of angina of effort has its origin in a perversion of function of the coronary artery or the muscle supplied by such artery. The argument that claims the pain in this accident is an aortic pain seems far-fetched. Even if the painful stimulus is transmitted by way of the aorta, the origin seems to be in the coronary artery or in the heart muscle. This does not imply that there may not be pain of anginal character having its origin in a diseased aortic wall.

Closer study of cases of angina pectoris and of coronary thrombosis with animal experimentation may help solve this problem. There may arise occasionally in connection with accident or surgery the opportunity of studying in man, in vivo and without an anesthetic, the effect of obstructing the coronary artery. Some cardiac Beaumont may find his Alexis St. Martin.

DEATH IN ANGINA PECTORIS DUE TO ACUTE CORONARY OCCLUSION

Sudden death is common in angina pectoris. How often is this due to the acute obstruction of a coronary artery? Probably the percentage of such deaths attributable to coronary obstruction will decidedly increase if careful autopsy investigation is made. LeCount's figures on coroner's cases are highly suggestive.

CRITERIA OF DIAGNOSIS

Generally easy to recognize if once thought of, this condition may be most perplexing. Are there helps to diagnosis that may be added to those already available? Critical and prompt decisions as to operation for suspected surgical accidents have to be made at times. Detailed reports of such cases will be helpful.

ATYPICAL CASES

Reference has already been made to certain variations from the type, especially as regards pain. Others might be mentioned. Dyspnea, often striking, merging into Cheyne-Stokes breathing may be present. Yet it may not be noticed. Blood pressure commonly drops, a most valuable symptom. Yet at times it holds up remarkably well, and unexplained daily or hourly striking variations in pressure are sometimes noted. The rate and rhythm of the pulse may be freakish. There may be little change from normal. The electrocardiogram may also be freakish. Dr. Walter Hamburger showed me the tracings in a hospital patient where extrasystoles from different foci, partial and complete block, paroxysms of tachycardia and of fibrillation had alternated with one another in an almost unbelievable manner during the several weeks following the seizure. Temperature is not always elevated. Subnormal temperatures have been reported. And there are other variations. This may increase the difficulties of diagnosis, but the study and reporting of these atypical cases will help establish rules for diagnosis.

TREATMENT

That rest and morphine do good or may save a life is generally believed. But how long in bed? What drugs? Is digitalis helpful or harmful? Does nitroglycerin do any good? Or do the theobromine compounds? Can anything be done to ward off an attack or a recurrence, e.g., by treating infections in one suffering from angina pectoris or from hypertension? Further careful observations like those of Levine on the helpful effects of quinidine, or of Allan on the use of glucose, are needed.

In conclusion to repeat what was said at the beginning, this paper is but an outline. It is intended to be suggestive. It is hoped it may stimulate to a further study of this interesting and important condition that is not yet by any means thoroughly understood.

FURTHER EXPERIENCES WITH VENESECTION IN CONGESTIVE HEART FAILURE*†

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In 1927 Eyster and Middleton[1] reported the results from venesection in a series of 21 cases of congestive heart failure. Their experience reaffirmed the value of this procedure in relieving right heart strain. Venous pressure determinations served as a guide to venesection in this clinical study, 20 cm. of water constituting the critical level, after the work of Clark.[2] It was furthermore established that the trend of the venous pressure curve subsequent to venesection served as an excellent measure of its efficacy. Almost invariably the venous pressure of the decompensated individual fell sharply on blood-letting. In the favorably reacting cases whose myocardial reserve was sufficient to meet the decreased diastolic load by a more adequate contraction, the venous pressure remained low and even tended to approach the normal level after the primary fall. On the other hand in the cases possessing an insufficient myocardial reserve, the temporary respite of a lessened diastolic filling was not adequate to initiate such a cycle. Hence the advantage of a lowered venous pressure from venesection was not maintained, and it thereafter mounted steadily to or above its previous level. Obviously such a distinction in the venous pressure curves following blood-letting in congestive heart failure must lend a considerable prognostic importance to such studies.

In the eighteen months elapsing since that report an additional group of 22 cases of congestive heart failure has been subjected to venesection. In addition to the usual subjective and objective criteria of right heart overload the determination of venous hypertension by the indirect method of Hooker and Eyster[3] again served as the final judgment. A venous pressure of 20 cm. of water, either maintained or ascending, was deemed adequate grounds for venesection. In Table I are listed the clinical data on the cases of this group.

An analysis of this table revealed a preponderance of cases with a myocardial degenerative background. Arteriosclerosis was the predominant etiological factor. The age grouping (9 in the fifth decade, 4 in the sixth and 9 over 60 years of age) undoubtedly determined this factor in a measure. Of the 22 cases only 3 were females. As to the remote and the recent occurrence of decompensation no relation was borne in the results from venesection.

A total of 26 venesections was performed on the 22 subjects; and in

*From the Department of Medicine, University of Wisconsin.
†Read before the Wisconsin Heart Club, April 19, 1929.

Table I.

No.	Age	Sex	Basic Lesion	Etiology	Occurrence-Decompensation		V.P. cm. H_2O	Amount Blood Let (cc.)	Resultant V.P.			Effect	
					Remote	Present			Lowest (cm. H_2O)	Interval	Duration	Immediate	Ultimate
1	47	M	Endocarditis	Rheumatic fever	3 years	3 mos.	18	550	8	Immediate	24 hrs. later 12 cm.	Improvement marked and immediate	13 days later V.P. 20 and return of cyanosis for short time; 17 days after venesection V.P. 7 and steady improvement in circulatory status
2	42	F	Endocarditis	Rheumatic fever	5 years	3 mos.	20	600	12	Immediate	24 hrs. later 16 cm. but fell to 12 on 4th day	Cyanosis cleared and there were fewer basal rales. General condition less affected	Steady improvement in general circulatory condition
3	72	M	Myocardial degeneration	Nephritis with hypertension	——	8 mos.	23	500	10	Immediate	Maintained for 2 days, then rose to 19 cm.	Early improvement objectively and subjectively	Hydrothorax reaccumulating led to repeated aspirations Death 42 days later
4	46	M	Myocardial degeneration; fibrinous pericarditis	Broncho-pneumonia; empyema	——	3 days	30	600	24	½ hour	9 hrs. later 20 cm.	Rallied slightly but anoxemia supervened	Oxygen controlled condition for time. Death 31 hours
5	53	M	Myocardial degeneration	Arteriosclerosis	——	4 mos.	24	500	14	½ hour	2 hrs. later 17 cm.	Cyanosis and dyspnea much improved	Improvement maintained for ten days
						Eleven days later	20	550	14	12 hours	?	Marked subjective improvement	Died 39 days after second venesection, apparently from effort of defecation. V.P. ran from 12 to 14 cm. in interval
6	74	M	Myocardial degeneration	Arteriosclerosis; hypertension	——	3 mos.	? edema	500	? edema	? edema	V.P. 14, 24 hrs. later	Pronounced relief in respiratory difficulty and pulmonary edema	Maintained improvement. Discharged 44 days later. V.P. ranged 8 to 14 cm. in interval
7	76	M	Myocardial degeneration	Arteriosclerosis; hypertension	2 years	3 mos.	26	500	10	Immediate	V.P. 16, 48 hrs. later	Remarkable improvement	V.P. ranged from 7 to 14 cm. until discharge 148 days later
8	50	F	Endocarditis; Myocardial degeneration	Rheumatic fever; hypertension	2 years	4 mos.	28	550	12	1 hour 20 min.	Maintained	Marked subjective improvement	V.P. 6 to 14 cm. until discharge 96 days later; convalescence not smooth, however.
9	41	M	Myocardial degeneration	Arteriosclerosis; bronchial asthma	——	7 mos.	18	500	8	½ hour	V.P. 12 cm. 24 hrs. later	Marked immediate relief	V.P. 10-15 cm. for 26 days and improvement maintained. On 27th day rise of V.P. with return of dyspnea and cyanosis
						Twenty-seven days later	18	600	9	35 min.	V.P. 14 cm. 4 days later	Much easier breathing and greater comfort	Steady higher level maintained after 4th day with general vascular slump, V.P. running from 12 to 23 cm. before death on 33rd day after 2nd venesection

TABLE I—CONTINUED

NO.	AGE	SEX	BASIC LESION	ETIOLOGY	OCCURRENCE DECOMPENSATION: REMOTE	OCCURRENCE DECOMPENSATION: PRESENT	V.P. CM. H_2O	AMOUNT BLOOD LET (CC.)	RESULTANT V.P.: LOWEST (CM. H_2O)	RESULTANT V.P.: INTERVAL	RESULTANT V.P.: DURATION	EFFECT: IMMEDIATE	EFFECT: ULTIMATE
10	69	M	Myocardial degeneration	Arteriosclerosis; hypertension	—	3 mos.	20	550	9	5 min.	24 hrs. later V.P. 12 cm.	Decided improvement in all details except psychic state	Objective and subjective improvement progressive and satisfactory until discharge 22 days later, highest V.P. 13 cm.
					Readmitted 122 days later		23	550	16	1 hour	Maintained	Much improved. Fell to sleep after procedure	Cyanosis and dyspnea relieved but V.P. only slowly fell to 7 cm. 11 days later
11	47	M	Endocarditis	Rheumatic fever	3 years	4 mos.	18	550	11	1 hour	Maintained for 2 days	Improvement objectively, Cheyne-Stokes respiration relieved	Two days later able to lie flat on back. V.P. 5-15 cm. until discharged 17 days later
									?	?	?	Slight improvement	Died in 24 hours
12	46	F	Endocarditis	?	—	10 mos.	22	500					
13	64	M	Myocardial degeneration	Arteriosclerosis; hypertension	—	2 weeks ?	20	510	14	2½ hours	Maintained	Relief of pressure sense in abdomen; cyanosis and dyspnea little affected	Died five days later
14	43	M	Myocardial degeneration	Hypertension	2 years	2 mos	23	500	14	Immediate	Fell to 8 cm. in 48 hrs.	Relief of dyspnea	Periodic dyspnea and pulmonary edema recurred. V.P. usually between 10 and 12 cm.
						Forty-one days later	? edema	475	? edema	—	—	No relief	Died 115 days later
15	64	M	Myocardial degeneration	Arteriosclerosis	4 years	3 mos.	?	520	10	Immediate	V.P. 21 cm. 2 days later	Early improvement in respiration, subjectively much better	Improvement not sustained, but after a period of 5 days slumped and died
16	63	M	Myocardial degeneration	Arteriosclerosis; hypertension	?	?	23	400	20	Immediate	—	No improvement	Died 6 hours later
17	62	M	Myocardial degeneration	Arteriosclerosis; hypertension	4 years	9 mos.	24	500	15	1 hour	24 hrs. later V.P. 14 cm.	Little change in general condition	Water balance remained poor, and subject died 10 days later of cerebral accident
18	43	M	Myocardial degeneration	Silicosis	4 years	4 mos.	24	500	8 ?	15 min.	Not maintained	No relief of pulmonary edema.	Died 4 hours later. Cyanosis and dyspnea unchanged by procedure and V.P. rapidly mounted
19	47	M	Endocarditis	Rheumatic fever	3 years	3 mos.	20	500	12	Immediate	12 cm. for 12 hrs; 14 next day	Marked improvement. Relief of cyanosis and dyspnea	Advantage held for 48 hours. Then V.P. rose to 18 but fell gradually and progress was satisfactory
20	50	M	Myocardial degeneration	Syphilis	1 year	6 mos.	? edema	500	? edema	—	—	Slight improvement in cardiac action	Death in 3 hours
21	62	M	Myocardial degeneration	Arteriosclerosis; hypertension	—	4 days ?	20	550	14	2 hours	6 hrs. later 16 cm.	Definite improvement in all details	In 48 hours further fall of V.P. to 10 cm. and continued progress; 2 thoracenteses apparently important in determining change
22	57	M	Myocardial degeneration	Arteriosclerosis	7 mos.	3 days	28	550	13	2½ hours	Maintained	Marked improvement	Marked diuresis on second day; V.P. remained low.

accord with the precept of Meek and Eyster[4] 500 c.c. of blood was, as a rule, withdrawn. On two occasions a somewhat smaller quantity was taken, but in 12 instances a larger amount was let. The immediate results were favorable in 11 of the 18 individuals who were bled a single time, and on 7 of the 8 occasions where a second phlebotomy was required in the remaining 4 subjects. Hence, it may be stated that the early response to venesection was satisfactory in 14 of 22 cases of congestive heart failure. An interesting correlation was established between the degree of venous pressure fall and the immediate clinical response to the procedure. Arbitrarily a fall of 8 cm. of water venous pressure was considered an adequate immediate response to venesection (500 c.c. of blood). On this basis 13 cases reacted favorably; and of these, a total of 11 showed definite clinical improvement. The corollary unfortunately does not hold; failure to effect an adequate fall in the venous pressure does not necessarily exclude a clinical advantage from the procedure, as witness cases 5 and 10 (second blood-letting) and 11 and 21 (single venesection).

The ultimate outcome of this group of 22 cases was quite illuminating. Only 10 individuals left the hospital. On the other hand, of the 12 cases terminating fatally, 5 survived the venesection by longer than a week, a limit which was arbitrarily set by Eyster and Middleton[1] as a fair indication of survival from the emergency which had led to venesection. The days of death after venesection in these cases were 42, 39, 33, 115, and 10, respectively. Two other cases survived 5 days and the remaining 5 fatal cases, 31, 24, 6, 4 and 3 hours, respectively. Clearly the last-mentioned group of 5 fatal cases (Nos. 4, 12, 16, 18 and 20) constitute a type in which hindsight might well condemn the plan of attack. It is interesting, too, that not a single case of this limited group showed early amelioration of right heart distress, and only 1 (Case 18) possibly fell in the group in which an adequate venous pressure fall was noted.

Characteristic clinical responses to venesection are abstracted in the following contrasting reports:

Case 4.—A white male, 46 years old, was admitted to the Wisconsin General Hospital, Feb. 6, 1929, with a history of a cough of 6 weeks' duration. Examination resulted in a diagnosis of bronchopneumonia with empyema (left). Three days later an accession of dyspnea and cyanosis was accompanied by a venous pressure of 30 cm. of water. A venesection was performed and 600 c.c. of blood let. Immediately thereafter the venous pressure reading was 27 cm. and in one-half hour the low level of 24 cm. was established. A subsequent rise to 26 cm. was recorded in another half hour. Although the evidences of anoxemia were partially controlled by oxygen, the circulatory balance was never restored, and the patient died in 31 hours after venesection. In addition to the anticipated pleuropulmonary changes, necropsy revealed a serofibrinous pericarditis, cardiac hypertrophy and dilatation and fibrous myocarditis.

Case 19.—A white male, 47 years old, was admitted to the Wisconsin General Hospital, March 23, 1929, complaining of dyspnea and weakness. A background

of rheumatic fever was established for the picture of cardiac decompensation, which included in addition to the subjective complaints above mentioned, generalized edema, nausea, vomiting, cough, cyanosis, congestive râles, cardiac enlargement, auricular fibrillation, hepatic engorgement, positive centrifugal venous pulse and ascites. A day's rest and medication failing to stabilize the circulatory condition and a venous pressure of 18-20 cm. of water pertaining, 500 c.c. of blood was withdrawn. During the course of the phlebotomy the patient expressed marked relief in the respiratory oppression, dyspnea subsided, and the cyanosis was lessened. Immediately after the venesection, the venous pressure registered 12 cm. of water and so remained for 12 hours. With but one temporary slump the advantage gained from venesection was maintained.

A comparison of results between the previously reported cases[1] and the present group would seem justified by the parallelisms in numbers, types, technic and controls. Eyster and Middleton[1] reported immediate improvement in 15 of 21 cases (71.4 per cent) as compared with 14 and 22 (63.6 per cent) in the present series. The ultimate results on the other hand indicate a more favorable response in the present group, 10 of 22 cases (45.4 per cent) surviving as compared with 6 of 21 (28.5 per cent). As in the earlier experience, a favorable primary response to venesection constituted a good prognostic sign, in that even the fatally terminating cases enjoyed a disproportionately extended length of life as compared with those showing no such immediate improvement after venesection. This rule held in all except Case 14 after the second venesection.

SUMMARY

In conclusion it may be granted that the immediate results from venesection of 500 c.c. in congestive heart failure are frequently spectacular and in a majority of instances, beneficial. From the very nature of the cases selected for this procedure ultimate recovery is not anticipated in a high proportion. Nevertheless, a survival of 45.4 per cent is reported in this group and an apparent prolongation of life claimed in an added 22.7 per cent (5 cases). The application of such a mechanical therapeutic measure as venesection offers a field of particular usefulness for venous pressure determinations, in that not only does venous hypertension constitute an index of right heart load, but the degree of primary fall in venous pressure on blood-letting and the curve thereafter serve as excellent prognostic measurements of its efficiency.

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THE USE OF CALCIUM CHLORIDE GIVEN INTRAVENOUSLY IN CONGESTIVE HEART FAILURE*

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IT HAS long been known that the presence of calcium ions is necessary to the function of contraction of heart muscle. Merunowicz[1] in 1875 first observed that the aqueous extract of ash when used as a perfusate would support contraction of the heart. It remained for Ringer,[2] however, to discover the necessity of the presence of calcium ions in the perfusion fluid. Following these observations, the study of ions in relation to the heartbeat was extended by Howell,[3] Loeb,[4] Burridge,[5] Mines[6] and others until it was finally established that the presence of calcium ions is necessary for the mechanism of contraction of heart muscle, while the presence of potassium ions is necessary for that of relaxation, and that the principal function of sodium ions is to maintain the proper relations of osmotic pressure. In the study of the pharmacological action of digitalis an attempt has been made to connect the action of digitalis with the presence of sodium, potassium or calcium ions. Clark[7] in 1912 published experiments on the perfused hearts of frogs which led him to conclude that the systolic action of digitoxin upon the frog's heart was dependent upon the presence of calcium ions, that diminution of the quantity of calcium in Ringer's solution diminished the systolic action of digitoxin while the presence of an excess of these ions did not influence the systolic action of digitoxin. Konschegg,[8] however, from data also obtained from perfusion experiments, came to an opposite conclusion, namely, that a strophanthin (digitalis) effect was not connected with the presence of calcium since the drug was still effective in hearts which had been washed free of this ion by prolonged profusion.

In 1917 Loewi[9] made a report of perfusion experiments bearing on this subject. He concluded that a strophanthin (or digitalis) effect consists only in making the heart muscle receptive to calcium ions; increased receptiveness is followed by an increased calcium effect. It is the function of digitalis bodies, in other words, merely to sensitize the heart muscle to the action of calcium which is already present in the circulating blood. He was of the opinion that the proportion of calcium was not lowered in cases of heart failure but that the sensitiveness of the heart muscle to the concentration of calcium present in the blood was diminished. Digitalis acts by restoring the sensitiveness of heart muscle to that concentration of calcium. The same result was

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said to be attainable if the level of calcium in the blood was temporarily raised by injecting calcium intravenously. Singer[10] on the basis of Loewi's experiments began injecting calcium chloride intravenously in the treatment of congestive heart failure. He reported excellent diuretic effects from its use. Later, he administered digitalis orally or intravenously simultaneously with the injection of calcium chloride intravenously. His results were striking in that diuresis amounting to from 7000 c.c. to 8000 c.c. per day was reported. Hellmann and Kollmann[11] confirmed these results in case of "Aortenfehlern" and "Myodegeneratio cordis." Loewenberg[12] observed similar effects following the intravenous injection of calcium chloride.

We are now reporting our experience with the intravenous injection of calcium chloride.

We have approached the problem from two points of view. In the first place we wished to ascertain whether calcium chloride in the amounts administered had an effect on the function of contraction of heart muscle in man, and in the second place we wished to test its diuretic effect in cases of congestive heart failure.

Before giving calcium chloride intravenously to patients we took the precaution of making preliminary observations on dogs with a view to learning the dose with which toxic effects on the heart were induced. We injected calcium chloride (10 per cent solution), 0.5 gm. to 1.1 gm., intravenously in dogs without the appearance in the electrocardiograms of ventricular premature contractions or ventricular standstill. In one dog we injected intravenously at the same time calcium chloride, 0.5 gm. and 30 per cent of the calculated lethal dose of tincture of digitalis (Upsher Smith). About forty minutes after the injection frequent ventricular premature contractions occurred and were still present one and one-half hours after the injection; they were no longer present the next day. One week later the experiment was repeated and similar results were obtained. One week later still, a smaller dose (25 per cent of the calculated lethal dose) of the same tincture was injected with the same amount of calcium chloride. In this case irregularity did not occur. A second dog was given 25 per cent of the calculated lethal dose of the tincture of digitalis intravenously without causing an irregularity. Two hours later calcium chloride, 0.5 gm., was given intravenously and ventricular premature contractions failed to develop. One week later, when 30 per cent of the calculated lethal dose was injected followed by the same amount of calcium chloride, a slight extrasystolic irregularity developed. It appears then that 30 per cent of the calculated lethal dose of digitalis is critical when combined with the injection of calcium chloride.

To study the effect of calcium ions on the functions of contraction we used the method of the moving x-ray films which was adopted by Cohn and Stewart[13] in their study of the effect of digitalis on contrac-

tion in the human heart muscle. This method consists in photographing with roentgen rays the excursions of the two borders of the heart. By this method continuous curves are obtained, the curves recorded representing the shortening or contraction undergone during systole by that portion of the left ventricular and right auricular margins which are photographed. The apparatus and technic of obtaining these curves has been described by Cohn and Stewart. These observations were made in male patients, the subjects of heart disease whose chests were reasonably thin and who were free of edema.

Preliminary moving x-ray photographs were taken at the level of the apex of the heart. This level was marked on the patient's chest. Immediately afterward the patient lay down and sterile calcium chloride (10 per cent solution) was injected intravenously. Moving x-ray photographs were then made at the same level as that at which the preliminary curve had been taken, the exposures being made at intervals ranging from two to thirty minutes after the injection. A series of such photographs was made of patients who had not received digitalis. In a second series of patients digitalis was given until by electrocardiograms (T-wave and conduction changes) and clinically (in auricular fibrillation slowing of ventricular rate) a digitalis effect was observed. After preliminary moving x-ray photographs were made of these patients, calcium chloride was given intravenously, and x-ray moving films were again taken, exposed as in the first instance. Both series of observations were made in patients in whom the rhythm was normal as well as in those who exhibited auricular fibrillation. Only those curves were measured in which the stationary films taken at the time the moving films were exposed showed that identical points on the left ventricular margin had been exposed in the photographs taken after injecting calcium chloride as had been exposed in the preliminary films. The excursions made by the heart's border were traced on tissue paper and the height of the left ventricular excursions measured in the manner described by Cohn and Stewart.[13]

The method of injecting calcium chloride was as follows. A venepuncture needle to which a Luer syringe was attached was inserted into a cubital vein. A small amount of blood was withdrawn in order to be certain that the needle had entered the vein. With the needle left in place this syringe was disconnected and one containing calcium chloride solution was substituted for it. Calcium chloride was injected slowly. The technic described avoids the danger of introducing calcium chloride into the subcutaneous tissues. If this occurs, necrosis of the tissues is said to take place. During injection the patients described a sensation of heat in the blood vessels as the calcium chloride was carried through the body. A few patients called attention to a salty taste. No untoward effects were observed either during or following injection. We have made studies of six patients; in four,

observations were made before they received digitalis and again after digitalis had been given. Of one patient, only, those photographs taken during the calcium chloride period were suitable for measurement, while of the sixth patient, the curves were measurable only in those photographs taken when calcium chloride was given at the time the patient was under the influence of digitalis.

A complete protocol is given in one case only.

CASE 1.—R. McCl. was a male, 18 years old. He complained of shortness of breath, weakness, loss of appetite and precordial pain of several months' duration. He had suffered from chorea in childhood. The tonsils were excised first when he was 6 years old. Frequent attacks of tonsillitis occurred from 1915 to 1920. There was an attack of acute rheumatic fever in 1916. In 1924 the tonsils were removed again. Since the last tonsillectomy there had been no attacks of acute tonsillitis. He was well from 1924 until the onset of the present illness.

Physical Examination.—The patient was a well-nourished, well-developed youth. He lay flat in bed without respiratory distress. There was no cyanosis. The teeth were in excellent condition. The tonsils had been cleanly removed. The heart was slightly enlarged. There were no thrills over the precordium; the heart sounds were essentially clear both at the apex and over the base, except for a presystolic element in the abrupt first sound. The second pulmonic sound was reduplicated. The heart rate was slow. The rhythm was regular except for occasional premature contractions which were followed by short compensatory pauses. The systolic blood pressure measured 100 mm. of mercury and the diastolic 70 mm. The lungs were clear. The abdomen was negative. There was no edema. The Wassermann reaction in the blood was negative. The urine was negative. The phenolsulphonephthalein excretion, the concentration and dilution tests for water excretion, and the index of urea excretion, all showed normal values. The leukocyte count varied between 11,000 and 15,000 when he was first admitted to hospital but later fell to 8,000. The count of the red blood cells was 7,000,000. The oxygen capacity of the blood was 10.28 mM. O_2, which is equivalent to 124 per cent hemoglobin. The electrocardiogram showed a normal rhythm and the conduction time was normal. There were occasional premature contractions.

On March 7, the patient was under the influence of digitalis; the left ventricular excursion at the level of the fourth interspace measured 5.2 mm. (Table I). Ten minutes after the intravenous injection of calcium chloride 0.5 gm. the excursion was 5.5 mm., that is to say it was substantially unchanged.

On March 9 the patient was still under the influence of digitalis; the left ventricular excursion measured 5.7 mm. Eleven minutes after calcium chloride, 0.6 gm., had been injected, it was 5.5 mm.; 22 minutes afterward it was 5.9 mm., that is to say the extent of ventricular contraction was unchanged. It may be recalled that 1 mm. is within the limits of error of measuring these curves. The patient received no digitalis for 10 days. On March 17 the excursion at the level of the fourth interspace was 5.4 mm. Ten minutes after the injection of calcium chloride, 0.8 gm., it was 6 mm., and 28 minutes afterward 6.4 mm. On April 10 when the patient was not under the influence of digitalis, the left ventricular excursion was 6.1 mm. The excursion was 5.9 mm. 6 minutes after the injection of calcium chloride, 0.8 gm., and 24 minutes afterward 7 mm. He was then given digitalis. On April 14 the left ventricular excursion was 7.2 mm.; 10 minutes after the injection of calcium chloride, 0.8 gm., it was 7.2 mm.; 20 minutes afterward it was 6.5 mm. It is clear then that calcium chloride did not increase the extent of contraction of the left ventricle either when it was given alone or when the patient was under the influence of digitalis.

TABLE I

EFFECT OF THE INTRAVENOUS INJECTION OF CALCIUM CHLORIDE UPON THE VENTRICULAR EXCURSION IN CASE 1. NORMAL RHYTHM

DATE	FILM NO.	INTERCOSTAL SPACE PHOTOGRAPHED	TRANSVERSE DIAMETER OF CONTROL FILM AT LEVEL PHOTOGRAPHED	ANALYSIS OF MOVING FILM: TRANSVERSE DIAMETER OF TRACING IN INSPIRATION: SYSTOLE	ANALYSIS OF MOVING FILM: TRANSVERSE DIAMETER OF TRACING IN INSPIRATION: DIASTOLE	ANALYSIS OF MOVING FILM: LEFT VENTRICULAR EXCURSION	ANALYSIS OF MOVING FILM: RIGHT AURICULAR EXCURSION	ANALYSIS OF MOVING FILM: HEART RATE	ANALYSIS OF STATIONARY FILM: CARDIAC AREA	ANALYSIS OF STATIONARY FILM: MIDDLE LINE TO LEFT BORDER	ANALYSIS OF STATIONARY FILM: MIDDLE LINE TO RIGHT BORDER	ANALYSIS OF STATIONARY FILM: TRANSVERSE DIAMETER	ANALYSIS OF STATIONARY FILM: LONG DIAMETER	ANALYSIS OF STATIONARY FILM: ANATOMICAL ANGLE	DIGITALIS	CALCIUM CHLORIDE INTRAVENOUSLY	TIME WITH REFERENCE TO INJECTION OF CALCIUM CHLORIDE
			cm.	cm.	cm.	mm.	mm.	per minute	sq. cm.	cm.	cm.	cm.	cm.	degrees	gm.	gm.	
March 7, 1925	i	4	11.5	11.8	12.6	5.2	3.1	120	94.0	7.6	4.0	11.6	13.2	41.0	+	0.5	Before
	ii	4	11.7	11.9	12.8	5.5	3.2	115	91.9	7.6	4.1	11.7	12.9	40.0			10 minutes after
March 9, 1925	i	4	12.0	12.5	13.4	5.7	3.9	96	97.5	8.4	3.9	12.3	13.9	35.0	+	0.6	Before
	ii	4	12.0	11.9	13.2	5.6	5.3	96	101.6	7.9	4.3	12.2	13.7	39.0			11 minutes after
	iii	4	12.5	12.5	13.5	5.9	4.0	96	109.7	8.0	4.6	12.6	14.1	40.0			22 minutes after
March 17, 1925	i	4	12.5	12.6	13.3	5.4	2.6	120	108.5	8.5	4.5	13.0	14.4	37.0	0 (none since 3/7/25)	0.8	Before
	ii	4	12.3	12.0	13.0	6.0	3.5	108	103.4	8.0	4.6	12.6	14.0	36.0			10 minutes after
	iii	4	12.0	12.5	13.5	6.4	2.9	108	93.0	8.0	4.1	12.1	13.9	38.5			28 minutes after
April 10, 1925	i	4	11.7			6.1		Time marker indistinct	94.2	8.2	3.7	11.9	13.9	34.0	0	0.8	Before
	ii	4	11.9			5.9			97.9	7.9	4.1	12.0	13.8	36.0			6 minutes after
	iii	4	12.5			7.0			103.0	8.3	4.3	12.6	14.2	37.0			24 minutes after
April 14, 1925	i	4	12.4	12.5	13.6	7.2	3.0	110	98.0	8.3	4.0	12.3	13.8	39.0	+	0.8	Before
	ii	4	12.7	13.0	14.4	7.2		96	100.3	8.3	4.3	12.6	13.6	35.0			10 minutes after
	iii	4	12.7	13.4	14.2	6.5	2.5	108	100.7	8.2	4.6	12.8	14.1	37.0			20 minutes after

TABLE II

SUMMARY OF THE OBSERVATIONS ON THE EFFECT OF CALCIUM CHLORIDE ON THE LEFT VENTRICULAR EXCURSION OF THE HEART

	RHYTHM	CASE NO.	NUMBER OF OBSERVATIONS	EFFECT ON LEFT VENTRICULAR EXCURSION	DIAGNOSIS*
Calcium chloride	Normal	Case 1	2	0	A: Acute rheumatic fever (inactive). B: Chronic myocarditis. C: Normal sinus rhythm; auricular premature contractions; cardiac pain.
		Case 2	1	0	A: Acute rheumatic fever (?). B: Cardiac hypertrophy; mitral stenosis and insufficiency; right ventricular preponderance. C: Normal sinus rhythm.
		Case 3	3	0	A: Acute rheumatic fever (inactive); chronic nephritis. B: Mitral insufficiency; cardiac hypertrophy; right ventricular preponderance. C: Normal sinus rhythm; arterial hypertension.
		Case 4 (Outpatient)	1	0	A: None. B: None. C: Normal sinus rhythm; cardiac pain.
	Auricular fibrillation	Case 5	4	0	A: Acute rheumatic fever (?). B: Mitral stenosis and insufficiency; aortic insufficiency; cardiac hypertrophy. C: Auricular fibrillation.
Calcium chloride and digitalis	Normal	Case 1	3	0	
		Case 2	1	0	
		Case 3	1	0	
	Auricular fibrillation	Case 5	5	0	
		Case 6	1	0	A: Acute rheumatic fever (?). B: Mitral stenosis and insufficiency; cardiac hypertrophy. C: Auricular fibrillation.
Total: Calcium chloride			11	0	
Calcium chloride and digitalis			11	0	

*The diagnoses conform to the nomenclature for cardiac diagnosis approved by the American Heart Association. AM. HEART J. 2: 202, 1926.
A = Etiological.
B = Anatomical.
C = Physiological.

Since the observations on all six patients yielded similar results they are not reported in detail. The data of all the patients are, however, summarized in Table II. Calcium chloride was given on seven occasions to four patients in whom the cardiac rhythm was normal and on four occasions to one patient the subject of auricular fibrillation. The extent of contraction of the left ventricle was not influenced by the drug in a single instance. It was given on five occasions

to three of the patients exhibiting a normal rhythm who had beforehand been given digitalis, and on six occasions to two patients, subjects of auricular fibrillation while under the influence of digitalis. In these instances also the injection of calcium chloride failed to induce a change in the extent of the left ventricular excursions. Since Cohn and Stewart[13] have shown that therapeutic doses of digitalis give rise to increases in the contractions of the left ventricle, we conclude that calcium chloride in the doses given does not affect the extent of contractions of the left ventricle, at least at the point of the ventricular margin which we studied.

There is, however, the possibility that calcium chloride might influence the force of ventricular contraction, although it does not affect the extent of contraction. Patients in whom the auricles are fibrillating lend themselves to the study of this phase of the problem. If

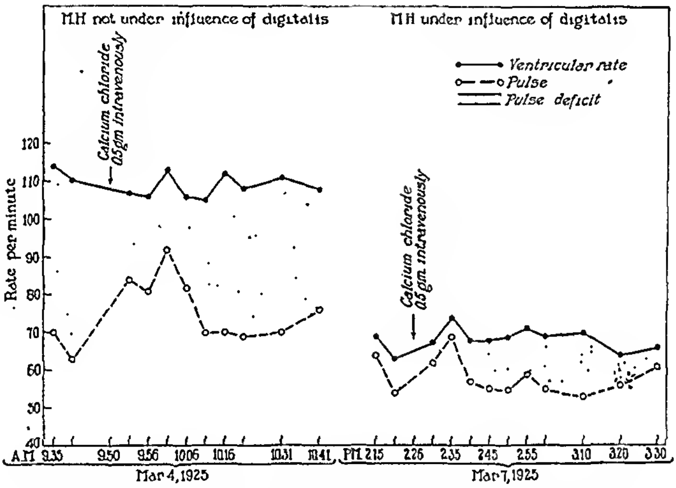

Fig. 1.—This shows the effect of intravenous injection of calcium chloride on the ventricular and on the radial pulse rate in Case 6.

the force of ventricular contractions increased following the injection of calcium chloride, a greater number of cardiac systoles may be forcible enough to open the aortic valves and to force blood into the vascular system; the pulse deficit will then be diminished. The patients studied from this point of view were at rest for one-half hour or longer. The ventricular rate at the apex and the pulse rate in one radial artery were counted simultaneously several times at intervals of a few minutes and the pulse deficit recorded. Calcium chloride was then given intravenously; the pulse rates were counted again at intervals of a few minutes until the end of one hour. These observations were made in several patients before digitalis was given and later also when the patients were under the influence of this drug. The injection of calcium chloride did not decrease the pulse deficit appreciably (Fig. 1); although it appeared that when the patient was not under the influence of digitalis and calcium chloride was injected, it was slightly

less for a few minutes after its injection, that is to say the number of effective beats was slightly larger; this effect, however, was only transitory. The results in the other patients were identical. No evidence is gained then from these observations that calcium chloride influences more than transiently the force of the ventricular contraction either if given alone or if given when the patient is under the influence of digitalis.

To ascertain the effect of calcium chloride upon the heart muscle three patients, subjects of auricular fibrillation, and three patients in whom the cardiac rhythm was normal were studied electrocardiographically. In two patients of each group observations were made when they were under the influence of digitalis as well as when they were not. They were given a preliminary period of rest varying from thirty to sixty minutes. Electrocardiograms were taken immediately before and at intervals of a few minutes after the injection of calcium chloride until the end of one hour. No changes were observed either in the form of the electrocardiogram, in conduction time in cases of normal rhythm or in the ventricular rate following the injection of calcium chloride.

There is then no evidence that calcium chloride in the doses given influences either the force or the extent of contraction of the heart, or that the heart muscle is affected by it, at least in respect to the observations which were made.

The use of calcium chloride administered intravenously as a diuretic.—Following Singer's[10] recommendation calcium chloride was given intravenously to twelve patients with edema of cardiac origin. All patients remained in bed until the effects of rest and of restriction of the intake of fluids had been established. Calcium chloride was then given intravenously both to those who were not and to others who were under the influence of digitalis; in a third set of observations digitalis was administered after the injection of calcium chloride. The report of these observations follows.

CASE 8.—G. E. This patient was a *male*, 58 years old. The cardiac diagnosis was as follows: *Etiological:* arterial hypertension; *anatomical:* cardiac hypertrophy, chronic myocarditis, slight right ventricular preponderance; *physiological:* normal sinus rhythm, congestive heart failure. The signs of congestive heart failure were hydrothorax and edema. The Wassermann reaction of the blood was negative. The systolic blood pressure measured 160 mm. of mercury and the diastolic 120 mm. The patient suffered a first attack of congestive heart failure one and one-half years ago. The present one was the third. Tremendous diuresis occurred when the patient was resting in bed and the fluid intake limited. It continued for many days. He became free of edema. When he began sitting up edema recurred. The patient was allowed to sit up the same number of hours each day. He was given calcium chloride, 0.1 gm., intravenously each night. On the fourth day there was a slight increase in the volume of urine. It was injected on four subsequent nights. The variation was no greater, however, than it had frequently been before the injection of calcium chloride. He was finally made free of edema by taking

digitan 0.5 gm. every 2 weeks and this state has been maintained even after he returned to work. It was in patients like this one that Singer thought the intravenous injection of calcium chloride particularly effective. Diuresis did not occur, however, in this instance.

CASE 9.—M. K. This patient was a male, 12 years old. The cardiac diagnosis was: *Etiological:* acute rheumatic fever (inactive); *anatomical:* mitral stenosis and insufficiency, tricuspid insufficiency, cardiac hypertrophy, right ventricular preponderance; *physiological:* normal sinus rhythm, congestive heart failure. The signs of congestive heart failure were edema, right hydrothorax, ascites and enlargement of the liver. This was the first attack of congestive failure. It was of one month's duration. Digitalis and theobromine diuretics were without diuretic effect. When the patient was not under the influence of digitalis, calcium chloride, 0.2 gm. a day, was given intravenously on 2 days; there was no increase in the volume of urine. The results were identical when the observations were repeated. The output of urine did not increase, and the patient became worse and died. An autopsy was performed. The diagnosis was: chronic cardiac valvular disease (mitral stenosis, aortic stenosis, tricuspid stenosis), verrucous endocarditis (mitral, aortic and tricuspid), septicemia (Streptococcus hemolyticus), fibrous pericarditis, fibrous pleurisy, general edema, ascites, hydrothorax, splenomegaly, infarcts of the lungs and the spleen, advanced chronic passive congestion of the organs, cirrhosis of the liver, calcification of the pancreas, fatty degeneration of the aorta, decubitus ulcers.

CASE 10.—A. B. This patient was a female, 44 years old. The diagnosis was: *Etiological:* acute rheumatic fever (inactive); *anatomical:* mitral stenosis and insufficiency, cardiac hypertrophy, right ventricular preponderance; *physiological:* normal sinus rhythm, congestive heart failure. The signs of congestive heart failure were ascites, enlargement of the liver, and edema. The patient had been the subject of chronic congestive heart failure for 20 months. During this time paracentesis had been performed every 3 weeks for relief of ascites. The first attack of failure occurred 3 years before. The usual measures were without effect in relieving the patient of edema and ascites. Calcium chloride, 0.1 gm. a day, was injected intravenously on 3 days. The output of urine did not increase. She was not benefited by the administration of digitalis, nor did diuresis occur when novasurol was given. She became worse and died. The autopsy diagnosis was: chronic cardiac valvular disease (mitral stenosis), ascites, hydropericardium, chronic passive congestion of the liver, spleen and pancreas, chronic peritonitis, perihepatitis, perisplenitis, cirrhosis of the liver.

CASE 11.—A. W. This patient was a negro, 71 years old. The diagnosis was: *Etiological:* arteriosclerosis, arterial hypertension; *anatomical:* cardiac hypertrophy, chronic myocarditis, left ventricular preponderance; *physiological:* normal sinus rhythm, congestive heart failure. The patient had suffered from two attacks of congestive heart failure. The first occurred 4 months before. The signs of congestive heart failure were right and left hydrothorax, ascites, enlargement of the liver, and edema. The Wassermann reaction of the blood was negative. The systolic blood pressure measured 223 mm. of mercury and the diastolic 134 mm.

The preliminary period before giving calcium chloride was not as well controlled as in the case of the other patients. While resting in bed the volume of urine increased. A water balance had not been reached under these conditions when calcium chloride was given. Calcium chloride, 0.2 gm., was injected intravenously on each of 4 days and 0.5 gm. on the fifth day. The volume of urine remained above the fluid intake on each of these days; the increase in output was not greater, however, than had been the fluctuations before calcium chloride was

given. At this time facial erysipelas developed and the patient died. The diagnosis at autopsy was: facial erysipelas, chronic myocarditis, fatty degeneration of the heart, cardiac hypertrophy and dilatation, hydropericardium, general arteriosclerosis, edema, ascites, hydrothorax, terminal pneumonia of the upper lobe of the right lung, anthracosis, arteriosclerotic kidneys, perisplenitis and perihepatitis, umbilical and inguinal hernias.

Summary.—In these 4 patients, then, diuresis did not occur as a result of injecting calcium chloride intravenously.

To eight patients calcium chloride was given in combination with digitalis. It was injected either before digitalis had been given, at the same time, or after the administration of digitalis.

CASE 12.—M. L. The patient was a male, 65 years old. The cardiac diagnosis was: *Etiological:* arteriosclerosis; *anatomical:* cardiac hypertrophy, chronic myocarditis, mitral insufficiency, aortic roughening, left ventricular preponderance; *physiological:* normal sinus rhythm, right intraventricular heart-block, congestive heart failure. Four attacks of congestive failure occurred in one year. The signs of failure were enlargement of the liver and edema. The patient remained in bed and was taking 1200 c.c. of fluid a day. The output of urine remained low. Calcium chloride, 0.5 gm., was injected intravenously. Increase in output did not occur. Since the patient was getting worse rapidly, digitan, 0.7 gm., was given within 9 hours. That day his output rose to 2843 c.c., and it was 5915 c.c., 3233 c.c., 2382 c.c., 1140 c.c., 1123 c.c., and 998 c.c., respectively on the succeeding 6 days. The patient lost 12.6 kg. in weight in 7 days; edema disappeared; the liver was no longer palpable. It was not necessary to give the patient more digitalis while he remained in hospital.

The observations in this patient were not satisfactorily controlled because he was acutely ill. When calcium chloride was injected intravenously one day followed by the administration of digitalis by mouth the next day, marked diuresis occurred. Several months later another attack of congestive failure occurred. On this occasion diuresis occurred when digitalis alone was given.

CASE 13.—P. P. This patient was a male, 51 years old. The cardiac diagnosis was: *Etiological:* arteriosclerosis; *anatomical:* chronic myocarditis, cardiac hypertrophy; *physiological:* auricular fibrillation, congestive heart failure. This was the first attack the patient had suffered. It had been present for one month. The signs of congestive failure were right hydrothorax, enlargement of the liver, ascites and edema. The systolic blood pressure measured 120 mm. mercury and the diastolic 80 mm. The patient was given digitalis. Moderate diuresis occurred. Two days later calcium chloride, 0.5 gm., was injected intravenously. The volume of urine diminished. Following the administration of digitan, 0.4 gm., the output increased slightly for 2 days. The increase in output was, however, no more than occurred following the administration of digitalis alone. The patient left the hospital against advice.

CASE 14.—S. C. (See Case 2, Stewart[14]). This patient was a male, 66 years old. The cardiac diagnosis was: *Etiological:* arteriosclerosis; *anatomical:* mitral insufficiency, cardiac hypertrophy, left ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. The signs of congestive failure were pulmonary congestion and edema. The patient had suffered from 3 attacks of failure in 5 years. The Wassermann reaction of the blood was negative. The systolic blood pressure measured 140 mm. mercury and the diastolic 80 mm.

This patient was kept under the influence of digitalis for 3 weeks. He was then given calcium chloride, 0.3 gm., 0.3 gm., and 0.1 gm., respectively on 3 days.

There was no increase in the output of urine. This is the patient in whom moderate diuresis occurred when calcium chloride was given by mouth. The patient died following an attack of acute cardiac dilatation. The diagnosis at autopsy was: general arteriosclerosis, chronic cardiac valvular disease, cardiac hypertrophy, aneurysm of the abdominal aorta, diffuse hyperplastic sclerosis of the kidneys and the pancreas, infarcts of the kidneys, terminal bronchopneumonia.

CASE 15.—M. de H. This patient was a male, 72 years old. The cardiac diagnosis was: *Etiological:* arteriosclerosis; *anatomical:* cardiac hypertrophy, mitral insufficiency, chronic myocarditis, left ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. The signs of decompensation were left hydrothorax, ascites, enlargement of the liver, and edema. The patient had suffered from two attacks of heart failure. The first occurred 4 years before. The systolic blood pressure measured 114 mm. of mercury and the diastolic 76 mm.

Calcium chloride, 0.2 gm., was injected intravenously on the same day that digitan, 0.5 gm., was given by mouth. The next day calcium chloride, 0.1 gm., and digitan, 0.2 gm., were given, and on the following day, calcium chloride, 0.1 gm. Diuresis did not occur. Later, when digitan, 2.1 gm., was given in 5 days, marked diuresis occurred, and the patient became free of the signs of congestive heart failure.

CASE 16.—D. di L. This patient was a male, 32 years old. The cardiac diagnosis was: *Etiological:* acute rheumatic fever; *anatomical:* mitral insufficiency, cardiac hypertrophy and dilatation, right ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. The signs of failure were ascites and edema. The patient had suffered from 2 attacks of heart failure. The first occurred 3 years before.

When digitalis was given, the volume of urine increased. While moderate diuresis was occurring, calcium chloride, 0.3 gm., was injected on 2 days and 0.2 gm. on the next 2 days; the administration of digitalis was continued. A further increase in the volume of urine did not occur. During the next 2 weeks calcium chloride, 0.3 gm., was injected for several days in succession, and the administration of digitalis continued. Diuresis did not occur. The patient became worse and died. The diagnosis at autopsy was: chronic cardiac valvular disease (mitral), verrucous endocarditis (tricuspid and aortic) calcification of the mitral valve.

CASE 17.—G. B. (See Case 4, Stewart[14].) The patient was a male, 69 years old. The cardiac diagnosis was: *Etiological:* arteriosclerosis; *anatomical:* aortic stenosis and insufficiency, mitral insufficiency, cardiac hypertrophy, left ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. The signs of congestive heart failure were right hydrothorax, enlargement of the liver, ascites and edema. This attack, the first that the patient had suffered, had been present for 6 months. Calcium chloride, 0.1 gm., 0.1 gm., and 0.2 gm., was given on 3 successive days. The volume of urine did not change. The administration of digitan, 0.5 gm., on the fifth day did not increase the output. Calcium chloride, 0.1 gm., was given on the seventh, and 0.2 gm. on the eighth days. Still it did not increase. On the day that digitan, 0.5 gm., was given a slight increase occurred. The administration of calcium chloride, 0.2 gm., on the eleventh and twelfth days, and of digitan, 0.5 gm., on the thirteenth day was not followed by diuresis. When calcium chloride and digitan were given in the same manner on the fourteenth, fifteenth and sixteenth days, increase in output again did not occur. The administration of digitalis was continued. One week later calcium chloride was given on 3 days (0.1 gm., 0.2 gm., and 0.2 gm., respectively). Diuresis did not occur. The patient died several weeks later. The diagnosis at autopsy was: general arteriosclerosis, chronic cardiac valvular disease (aortic), perforation of the intraventricular

septum, contraction of scar in the conus of the pulmonary artery, hypertrophy and dilatation of the right and left ventricles, chronic myocarditis, venous congestion of the organs, arteriosclerotic kidneys, cysts of the kidneys.

CASE 18.—S. F. (See Case 1, Stewart[14].) This patient was a female, 24 years old. The cardiac diagnosis was: *Etiological:* acute rheumatic fever (inactive); *anatomical:* mitral stenosis and insufficiency, aortic insufficiency, cardiac hypertrophy, left ventricular preponderance; *physiological:* auricular fibrillation, congestive heart failure. The patient had suffered from 3 attacks of failure. Edema was present and the liver was enlarged. She had been in hospital for many months. The administration of digitalis was followed by slight diuresis, but it was not sufficient to free the patient of edema. Calcium chloride, 0.1 gm. a day, was given intravenously on 5 days. Diuresis did not occur. On the sixth day, the administration of digitan, 0.9 gm., was not followed by a greater diuresis than had occurred on previous occasions when its administration had not been preceded by the injection of calcium chloride. The effect of digitalis was allowed to wear off. Calcium chloride, 0.1 gm. a day, was given on 6 days; increase in output did not occur. On the eighth day, digitan, 0.5 gm., was given; slight diuresis occurred. On a third occasion when calcium chloride, 0.1 gm. a day, was given for 2 days followed by digitan, 0.5 gm., a change in output likewise did not occur. On a fourth occasion, calcium chloride was given in 0.1 gm. doses on 8 days; the volume of urine did not increase. Now when on the ninth day digitan, 0.5 gm., was given, no greater output occurred than was expected from giving digitalis alone.

In short when calcium chloride was injected intravenously alone, diuresis did not occur. When the injection of calcium chloride was followed by the administration of digitalis the increase in output was no greater than occurred when digitalis was given alone.

CASE 19.—O. M. The patient was a male, 44 years old. The cardiac diagnosis was: *Etiological:* hypertension, acute rheumatic fever (13 years before), syphilis (Wassermann reaction positive); *anatomical:* mitral insufficiency, aortic insufficiency, cardiac hypertrophy, left ventricular preponderance; *physiological:* normal sinus rhythm, congestive heart failure. Four attacks of heart failure had occurred within 2 years. The signs of failure were hydrothorax, ascites and edema. The systolic blood pressure measured 190 mm. of mercury and the diastolic 60 mm. The administration of theocalcin (Merck) was followed by satisfactory diuresis. When digitan was given in doses sufficiently large to affect the form of the T-waves of the electrocardiograms, increase in the volume of urine did not occur. When the patient was no longer under the influence of digitalis, calcium chloride, 0.5 gm., was injected intravenously. The next day he was given digitan, 0.9 gm., the next day 0.4 gm., and on the following day 0.1 gm. Diuresis did not occur. The patient became free of edema after several months. This end was attained by limiting the fluid intake and by the administration of theocalcin and digitalis. While in hospital dullness on percussion and râles on auscultation appeared in the left side of the chest in front. At the same time a shadow was seen in the x-ray photograph of the chest. A diagnosis of tumor of the lung was made. It increased in size very rapidly, and the patient died of carcinomatosis two months later. The diagnosis at autopsy was: carcinomatosis of left lung, liver and lymph glands, chronic passive congestion of the left kidney; hydronephrotic contraction of the right kidney. The heart on gross examination appeared normal.

Summary.—When calcium chloride combined with the administration of digitalis was given intravenously to 8 patients suffering from congestive heart failure, diuresis did not occur except in one instance

(Case 12). In this case there is doubt whether calcium chloride played a part in inducing diuresis.

SUMMARY

As has already been stated we could obtain no evidence by the methods we employed that calcium chloride in the doses given influenced either the force or the extent of contraction of the heart. Furthermore, when it was given to 12 patients with edema a diuretic effect was not observed. Nor did diuresis occur when the injection of calcium chloride was combined with the administration of digitalis. In one patient (Case 12) in whom the observations were not satisfactorily controlled, there occurred striking diuresis when digitalis was given twenty-four hours after the injection of calcium chloride. There is reason from a later experience with this patient for thinking, however, that calcium chloride played no part in initiating diuresis. Increases in output did not occur when calcium chloride was given to patients who were not suffering from congestive heart failure.

DISCUSSION

In only one of our cases did we observe, following the intravenous injection of calcium chloride, such a striking effect as Singer reported. In this instance it is not certain that calcium chloride played a major part. In the other cases diuresis did not occur. Most of the patients were those in whom all the measures employed were without effect in removing the fluid from the subcutaneous tissues and serous cavities; in most instances progression of heart failure continued until death occurred. Two, however (Cases 8 and 15), responded readily to other drugs (digitalis, theocalcin). We did not inject doses larger than 1 gm. Salvesen, Hastings and McIntosh[15] have shown that if this amount of the salt is injected into dogs the amount of calcium in the serum of the blood increases 30 to 31 per cent shortly after injection and returns to normal four to six hours later. It may be that when this amount of calcium chloride is distributed through the much greater volume of fluid which is present in man, that it is so diluted as not to raise appreciably the level of calcium concentration of the blood.

That this amount of calcium chloride has an effect on the hearts of dogs was shown in our preliminary experiments; in these we demonstrated that 30 per cent of the calculated lethal dose of digitalis when combined with calcium chloride gave rise to ventricular premature contractions, while 25 per cent of the calculated lethal dose may be injected simultaneously with calcium chloride without the appearance of premature contractions. We observed no effect, however, on the heart when 1 gm. of the salt (calcium chloride) was given to patients, whether they were or were not under the influence of

digitalis at the time of the injection. There was no increase in the extent of left ventricular contraction, in the force of ventricular contraction and no effect on the heart muscle that could be detected electrocardiographically. If doses were given to patients comparable to those given to dogs, effects might have been detected by the methods we employed. It did not seem wise, however, to inject larger amounts, since Singer observed striking results when only 0.1 gm. of the salt was injected alone or when this amount was combined with extremely small doses of digitalis. In the one patient in our series (Case 12) in whom diuresis occurred, it is uncertain, as has already been stated, whether this result was connected with the preliminary injection of calcium chloride. On a subsequent admission excellent diuresis occurred when digitalis alone was given. From our experience with digitalis and from our present experience with calcium chloride it seems unlikely that calcium chloride played a rôle in initiating the diuresis that occurred.

CONCLUSIONS

1. Calcium chloride when injected intravenously in man in amounts as large as 1 gm. had no effect on the extent of contraction of the left ventricle (method of the moving x-ray film); it was without effect on the force of contraction of the heart (if the number of effective beats in patients suffering from auricular fibrillation is used as a criterion); and it had no effect on the electrocardiograms. These were the results whether the patient was or was not under the influence of digitalis when calcium chloride was injected.

2. The injection of calcium chloride intravenously into patients suffering from congestive heart failure in doses varying between 0.1 and 1 gm. did not result in diuresis. Digitalis did not appear to be more effective as a diuretic in these patients when it was combined with calcium chloride than when it was given alone.

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DIGITALIS TOLERANCE OF PATIENTS SUFFERING FROM RENAL INSUFFICIENCY*

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The clinical impression has been prevalent that patients suffering from renal insufficiency do not tolerate digitalis well.[1, 2] It has been believed that patients rapidly cumulate the drug and that digitalis intoxication occurs after the administration of small doses. The present observations were undertaken to test the validity of this conception.

Ten patients diagnosed as having chronic glomerular nephritis with varying degrees of renal insufficiency were chosen as subjects for this study. All patients were in hospital, and none had received digitalis previously during the hospital admission. The diagnosis of chronic glomerular nephritis was made on the history of a chronic illness, the presence of a secondary anemia, and on the urinary findings (pale urine, fixed low gravity, containing albumin, with casts and red blood cells). All patients had impairment of renal function as indicated by the retention of protein metabolites in the blood. The laboratory data are summarized in Table I. Electrocardiograms were taken before digitalis was given. The usual leads were employed, and all records were taken after customary standardization of the string. (Introduction of 1 millivolt—1 cm. deflection.) Digitalis was administered as the U. S. P. tincture of known potency and in doses comparable with clinical practice, viz., 1.3 c.c. three times daily. This dosage was chosen additionally because Cohn, Fraser, and Jamieson used like

Table I

PATIENT	AGE	P. S. P. 2 HR.	UREA MG. PER 100 C.C.	TINCTURE OF DIGITALIS ALTERING T-WAVE	EQUIVALENT DOSE OF POWDER	TIME TO FIRST CHANGE OF T-WAVE	TOTAL DOSAGE	SYMPTOMS WITH DOSAGE
A. M.	20 years		268	9.3 c.c.	0.93 gm.	24 hrs.	64.0 c.c.	None
R. L.	44 "	17%	157	6.6 c.c.	0.66 gm.	16 hrs.	20.0 c.c.	Vomited 20.0 c.c.
L. B.	41 "	15%	259	8.0 c.c.	0.8 gm.	48 hrs.	14.6 c.c.	Vomited 14.6 c.c.
A. C.	28 "	15%	380	28.0 c.c.	2.8 gm.	6 days	28.0 c.c.	Vomited 28.0 c.c.
S. H.	64 "	23%	151	8.0 c.c.	0.8 gm.	2 days	26.6 c.c.	Vomited 26.6 c.c.
J. A.	49 "	35%	114	9.3 c.c.	0.93 gm.	2 days	15.3 c.c.	Vomited 15.3 c.c.
A. R.	40 "	30%	74	6.0 c.c.	0.6 gm.	2 days	21.0 c.c.	Vomited 14.6 c.c.
S. S.	47 "	7%	276	12.0 c.c.	1.2 gm.	3 days	20.0 c.c.	None
A. D.	36 "	0	341				28.0 c.c.	None
A. R.	35 "		38	12.0 c.c.	1.2 gm.	2 days	21.3 c.c.	None

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amounts in their study of the effects of digitalis on the T-wave (0.4 gm. digipuratum daily). The results of this study then can be compared with the results of their observations. The physiological effect of the drug was noted clinically (loss of appetite, nausea, vomiting) and electrocardiographically (flattening and inversion of the T-wave).

RESULTS

Ten patients with glomerular nephritis were given 1.3 c.c. tincture of digitalis three times daily until electrocardiographic evidence of digitalization occurred or until clinical symptoms of intoxication were noted. The first definite alteration in contour of the T-wave was noted, and this early change was checked with later marked alteration in contour. From 6.6 c.c. to 12 c.c. were given before the T-wave altered. In one instance 28 c.c. were given before change in the T-wave occurred. The total amount of digitalis taken varied from 14.6 to 64 c.c. In the last column is noted the amount of digitalis which was necessary before nausea or vomiting occurred. The latter symptoms could not be observed in one case because of the presence of nausea before the administration of digitalis.

DISCUSSION

The amount of digitalis required to induce intoxication was first studied by Withering.[3] He wrote that "about thirty grains of the powder or eight ounces of the infusion may generally be taken before the nausea commences." He gave one to three grains of the powder twice daily. This observation is one in which most clinicians will concur. It will be seen in Table I (last column) that the total dosage required to cause nausea varied from 14.6 c.c. to 26.6 c.c. (21.9 to 39.9 grains). Cohn, Fraser, and Jamieson[4] noted that the T-wave in the electrocardiogram was usually inverted after the administration of digitalis. They noted also a variation in the amount of digitalis causing this change. With a usual daily dose of 0.4 gm. of digipuratum the first change in T-wave was seen as early as from 36 to 48 hours after the onset of therapy. The inversion of the T-wave in their series lasted from 5 to 22 days after the drug had been stopped. In two of our cases the T-wave returned to normal in 12 and in 20 days respectively. Bromer and Blumgart[5] recently noted a great variation in the amount of digitalis required to alter the T-wave.

CONCLUSION

It will be seen that these ten patients with impaired renal function, from moderate to considerable degree, tolerated digitalis well. The amounts of digitalis necessary to alter the T-wave in the electrocardiogram were no less than cardiac patients usually require. This observation was confirmed by clinical evidence as well.

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THE VELOCITY OF BLOOD FLOW IN HEALTH AND DISEASE AS MEASURED BY THE EFFECT OF HISTAMINE ON THE MINUTE VESSELS*†

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INTRODUCTION

THE velocity of the blood flow is an important characteristic of the circulation.[1, 2] In different individuals under similar conditions variations are relatively slight, while in various pathological states of the circulation considerable deviations from the normal are present. The variations from the normal often parallel the degree of circulatory insufficiency. Measurement of the velocity of blood flow along the important pathways is, therefore, serviceable in evaluating objectively the efficiency of the circulation. It is of considerable practical importance that measurement of the velocity of blood flow should demand little cooperation on the part of the patient. The results of a number of methods for the measurement of various aspects of the circulation are of doubtful value because their proper application depends upon full cooperation of the patient.

All methods used in the past for the measurement of the velocity of blood flow in man consist in the injection of a relatively indifferent substance into a peripheral vein and the determination of the time elapsing between the injection and the arrival at another designated part of the vascular system. This arrival time has been determined: *A*, by the appearance of the color of the injected substance in the serum following arterial or venous punctures (fluorescein);[3] or *B*, by registration of change in the conductivity in the blood as a result of the arrival of an injected electrolyte. Concentrated salt solution has been injected intravenously, and an electrode through the skin has been inserted next to the radial artery,[4] or into the cubital vein.[5] The arrival of the salt solution in the corresponding part of the vessel has been registered with the aid of a galvanometer. *C*, a third method used for the measurement of the circulation time is that of injecting a small amount of nontoxic radio-active substance intravenously and detecting its arrival in one or several parts of the vascular system by specially constructed detectors which are sensitive enough to register the direct radiation of the active deposit when the latter arrives at the part of the vessel

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under observation.[6, 7, 8] Each of these methods offers certain advantages over the others, depending on the purpose of the inquiry.

THE PROBLEM

While engaged in a study of the effect of the intravenous administration of histamine on the peripheral part of the vascular system of normal individuals,[9] it was observed that the onset of facial flush followed the injection of histamine at a quite definite and regular interval, and that the onset of the flush was rather sharp and easily detectable. It was thought that the time interval elapsing between the injection into the antecubital vein and the appearance of the flush might express the time necessary for a particle of blood to progress from the antecubital vein into the small vessels of the face.*

Attempts to measure the circulation time with the administration of chemical substances which exert a definite effect on some easily observed physiological function are few. Loevenhart, Schmolovitz and Seybold[11] determined the circulation time of the rabbit and the cat by injecting sodium cyanide intravenously. Sodium cyanide, as is well known, stimulates the respiratory center, and so the period elapsing between the injection and the appearance of increased respiration was used as a measure of the circulation time. The circulation time obtained by this method in rabbits corresponded closely to that obtained with ferrocyanide, hexamethylene tetramine and lithium chloride. In cats the reaction time to sodium cyanide was slower than the circulation time obtained by the other methods.

Bornstein[12] administered one deep breathful of air containing between 5 and 7 per cent of carbon dioxide to normal subjects and to patients, and the time interval between the inhalation of the carbon dioxide and the appearance of the first deep inspiration was used as an expression of the circulation time between the capillaries of the lung and of the respiratory center. Bornstein recognized that this method was inaccurate and that its application was greatly limited by the variability in the response of the respiratory center to carbon dioxide in many pathological conditions. According to him, the circulation time observed under such experimental conditions was about half of the cubital vein to cubital vein circulation time. As far as we know, only short preliminary reports appeared on these two attempts.

The application of a chemical substance which exerts a definite and easily detectable change on a bodily function offers the great advantage for the measurement of the circulation time because of its extreme simplicity. To use a substance for such a purpose the following prerequisites should be fulfilled:

1. The substance must not be toxic in the amounts utilized.

*Harmer and Harris[10] administered intravenously small amounts of histamine in a few instances.

2. The substance should not influence the velocity of the blood flow during the first circuit of its flow following the injection.

3. The substance and its effect on the body should disappear rapidly, so that the test can be repeated at short intervals.

4. The reaction time of the substance after its arrival in the tissues where the proper changes are expected should be short.

5. The change in the function of the body which is used as a signal of the arrival of the substance should occur both in normal and in pathological conditions of the body, and should be detected easily.

The time which elapses between the injection of a substance and the detection of the signal sign (flush, respiratory effect, etc.) includes the circulation time, and also the time necessary for the effect of the chemical agent to manifest itself following the arrival of the substance in the small blood vessels (capillaries). This latter period (the time elapsing between the arrival of the substance into the capillaries and the manifestation of its action) should be called the reaction time proper of a substance. This reaction time is more uniform than the "reaction time" which includes the entire period from the time of injection until the manifestation of the physiological change. Nevertheless, hereafter the term reaction time is used as the time which elapses between the injection of histamine and the onset of flush as observed.

PLAN OF INVESTIGATION

The intensity of the pharmacodynamic effect of a substance depends on the concentration in which it comes into contact with the tissues. It was expected, and found by experience, that the smaller the volume and the greater the concentration of the histamine solution injected, the more definite and intense was the facial flush. The injection of a small volume also had the advantage of not changing the blood volume in any appreciable amount. The application of histamine in increased concentration was limited by its undesirable effect on the body. After the administration of relatively large doses, a marked rise in the cardiac rate, occasional marked fall in the blood pressure, sensation of weakness, headaches, nausea and vomiting were observed. After some experience it was found that the sudden injection of 0.001 mg. of histamine phosphate per kilogram of body weight in a concentration of 1:10,000 or 1:5000 regularly produced marked flush of the face in white individuals. Almost simultaneously with the onset of flush, a sensation described as "salty," "metallic," "electric" is felt in the tongue of the subject. This sensation offers a check for the observation of the color. In the later part of our investigation we used the concentration of 1:5000 of a solution of histamine phosphate, 0.35 c.c. being used in an average man of 70 kg.* The injection was made suddenly

*All doses are expressed in terms of histamine phosphate.

from a finely gradnated Luer syringe. The time of the injection and the onset of flush and taste were registered with a stop watch. Good direct daylight facilitated the recognition of the flush.

To ascertain whether the time obtained under such an experimental condition corresponded to the true circulation time, and to gather evidence as to whether the procedure was feasible for practical application, the following observations were made.

The reaction times of a large number of normal subjects and of patients were studied, and the results were compared with the circulation time obtained on another group by the radioactive deposit method. To compare the results of the two procedures in the same individual under identical conditions, the histamine reaction time and the circulation time by the radioactive deposit method were determined simultaneously in normal persons and in patients with cardiovascular disease. To ascertain whether the histamine circulation time could be repeated at short intervals, tests were made on the same individuals at short intervals. To observe the effect of the intravenously administered histamine on the circulation, the cardiac rate was measured by electrocardiographic tracings taken during and after the measurement of the circulation time. Similarly repeated blood pressure determinations were carried out during and after the test. As the pharmacodynamic action of histamine produces marked effects on the small vessels, it was important to learn whether the drug exerted any definite effect on the pulmonary arterioles, capillaries and venules. If such an effect were present, it might alter the circulation, the very thing to be measured. Direct observations on the effect of histamine on the pulmonary capillaries of man are not feasible. For this reason direct observations were made on the pulmonary capillaries in the cat.[13] No definite changes were observed in the behavior of the pulmonary capillaries. In addition, the pulmonary circulation time of normal subjects and of patients was measured following the injection of histamine.

OBSERVATIONS

The Reaction Time of Histamine in Normal Individuals.—Histamine phosphate, in amounts of 0.001 mg. per kg. of body weight in 1:5000 or 1:10,000 solution, was injected into the antecubital vein of 65 normal subjects, and the reaction time on the small vessels of the face was determined. The ages of these individuals varied from fourteen to sixty-nine years. All tests were performed with the subjects in the recumbent position after their confidence and cooperation had been obtained. The findings are summarized in Table I, according to the age incidence of the subjects. In 65 normal subjects the reaction time between the cubital vein and the small vessels of the face varied between 13 and 30 seconds; the average circulation time was 23 seconds. It is of interest that the arm to arm circulation time in 53 normal individu-

als measured by the radium active deposit method, varied between 14 and 24 seconds; the average circulation time was 18 seconds.[8] The slightly more prolonged reaction time obtained by the histamine method is probably explained by the fact that the histamine method measures the time necessary for the arrival of the blood to the capillaries, while the radioactive deposit method measures the time of arrival of the blood in a large artery (cubital artery). It is known that the blood flow slows down considerably in the smaller vessels. E. Hering[14] estimated the capillary circulation time to be 5 seconds. Koch[3] observed in one subject the appearance of fluorescein in the cubital artery in 10 seconds, while the dye was detected in the cubital vein in 18 seconds, corresponding to a capillary circulation time of 8 seconds. We observed even greater difference between the arterial and venous circulation times with the fluorescein method.[8] The time

TABLE I

THE REACTION TIME OF HISTAMINE IN SIXTY-FIVE NORMAL INDIVIDUALS

AGE	NO. OF SUBJECTS	AVERAGE HEART RATE	AVERAGE BLOOD PRESSURE SYSTOLIC	DIASTOLIC	REACTION TIME MINIMAL	MAXIMAL	AVERAGE
Years			mm. Hg.	mm. Hg.	seconds	seconds	seconds
10-19	12	82	118	64	13	22	18
20-29	16	80	116	72	14	30	21
30-39	13	84	124	76	15	29	23
40-49	10	78	128	80	20	30	25
50-59	7	80	134	84	17	22	20
60-69	7	84	138	88	21	27	25

which elapses between the arrival of histamine in the small facial vessels and the appearance of flush, may also be a factor in the difference between the results obtained with the two methods. It should be remembered, however, that the two procedures applied measure the circulation time between two different parts of the body which may be different even when measured with the same method.

With the onset of the flush there was a subjective sensation of heat over the face and tension in the head which lasted from 1 to 3 minutes. There was a period of from 15 to 30 seconds after the onset during which the flush increased in intensity. The flush was localized over the face and neck, the rest of the body showing a flush in but few instances. The total duration of the flush was from 12 seconds to 2 minutes. With the onset of flush the cardiac rate increased. The duration of increased cardiac rate, as a rule, went parallel with the duration of flush. Its height was reached in about 15 to 60 seconds after the onset of the flush. The maximum rise in the heart rate was from 15 to 20 beats a minute. Blood pressure, as a rule, showed but little change during and after the flush. A definite fall was not obtained. A slight rise of 10 to 20 mm. Hg., in the systolic and diastolic pressures, during and immedi-

ately after the flush, was observed frequently. With the return of the cardiac rate to normal the blood pressure likewise became normal again. A number of patients complained of throbbing headaches which began 10 to 20 seconds after the onset of the flush and lasted usually from 3 to 10 minutes.

The Relation of the Onset of the Increased Heart Rate to the Onset of Flush.—The intravenous injection of histamine in the amounts described was always followed by an elevation of cardiac rate. In order that the histamine reaction may be used for the measurement of the velocity of blood flow, it is essential that the very characteristics of the circulation to be measured should not change. Although change in the heart rate does not necessarily imply change in the velocity of blood flow, it is desirable that the increase of the cardiac rate should not occur before the onset of flush. Numerous observations indicated that the onset of increased cardiac rate was coincident with the onset of flush and sensation of taste. In order to study this aspect of the problem in a more exact way, the cardiac rate of normal subjects and patients suffering from circulatory failure was registered continuously by Lead II of the electrocardiographic machine. At the moment of injection and at the appearance of flush the string of the galvanometer was temporarily short circuited. The cardiac rate was registered 30 to 60 seconds after the onset of flush. The analysis of the records indicates that in 8 of 14 observations acceleration of the cardiac rate was increased with or immediately after the onset of flush. In 6 observations there was a slight increase in rate by 2 and 3 seconds before the onset of flush. It is of interest that a number of subjects showed temporary inversion of the T-wave for from 20 to 60 seconds. This inversion of the T-wave with the acceleration disappeared as the rate returned to normal.

The observation that with the increase of rate there was a depression of the T-wave suggests that the increase of rate is the result of the effect of histamine on the coronary vessels of the heart and that this increase of rate begins simultaneously with the flush, or 2 to 3 seconds before it is noted.

Repeated Tests in the Same Individuals.—Repeated tests were performed on a number of individuals to ascertain the difference in repeated measurements, and to determine how soon the test could be repeated. The flush, changes in heart rate and in blood pressure suggested that the persistence of the effect of a single intravenous dose of histamine is of short duration, and that the test could be repeated within a few minutes. Observations substantiated this expectation. Table II presents a few of our findings in normal individuals and in patients.

The average variations were not more than 2 to 3 seconds. The findings presented in Table II indicate that the test can be repeated within 5 and in some cases even within 3 minutes. In patients with circulatory failure, especially when this is due to myocardial degeneration

TABLE II

REPEATED ESTIMATION OF THE REACTION TIME OF HISTAMINE IN THE SAME PERSON

DATE	NAME	AGE	CONDITION	PULSE	HIST. PH. PER KG. OF BODY WEIGHT	REACTION TIME	TIME INTERVAL BETWEEN REPETITION OF TESTS	DIFFERENCE BETWEEN REACTION TIMES
1928		(years)			mg.	Sec.	Min.	Sec.
4-4	T. D.	24	Diabetes	70	0.0010	20	9	0
				78		20		
4-4	T. M.	19	Bronchitis	68	0.0011	17	12	1
				76	0.0011	16		
4-4	T. G.	18	Normal	72	0.0011	18	3	1
				72	0.0011	17		
4-5	N. F.	48	Normal	78	0.0003	23	11	0
				76	0.0008	23		
				80	0.0012	24	6	1
				76	0.0015	24	3	1
				72	0.0017	23	3	0
5-22	A. K.	28	Post. Pneum.	74	0.0007	35	13	6
				72	0.0010	29		
4-5	P. R.	63	Emphysema	63	0.0008	26	7	2
					0.0011	24		
6-16	R. M.	41	Arterial hypertension	84	0.0010	28	3	2
				86	0.0010	30		
4-21	H. T.	45	Aortic insufficiency	96	0.0009	29	6	1
				104	0.0009	28		
4-7	S. S.	75	Arteriosclerosis	96	0.0009	37	13	3
				92	0.0007	40		
4-13	J. F.	75	Myocardial degeneration	110	0.0005	45	7	4
			Auricular fibrillation	104	0.0008	49		
5-5	P. M.	54	Myocardial degeneration	100	0.0011	59	11	17
				100	0.0011	42		
5-10	L. E.	56	Myocardial degeneration	72	0.0011	64	9	7
				88	0.0008	57		

and arteriosclerosis, the variations were considerably higher. The duration of the flush, as well as the change in heart rate and subjective sensation, lasted longer in these patients than in normal individuals. We believe that this greater variation in the results is due, at least partly, to fluctuations in the velocity of blood flow. In patients with circulatory failure it is advisable not to repeat the test within 10 minutes. As the observation on patient N. F. indicates, the amount of histamine can vary considerably without change in the circulation time. The minimal effective dose is about three times smaller than the dose usually applied.

Simultaneous Measurement of the Histamine Reaction Time and the Circulation Time by the Radioactive Method.—The measurements described indicated that the histamine reaction time in normal individuals corresponds closely to the arm to arm circulation time, as measured with the radioactive deposit method. For a more definite establishment of the significance of the histamine reaction time, simultaneous measurements with the two methods were performed both on normal individuals and on patients suffering from cardiovascular disease. For this purpose the amount of radioactive deposit required for the measurement of the circulation time and the histamine were dissolved

TABLE III

COMPARISON OF CIRCULATION TIMES AS DETERMINED BY THE RADIUM AND HISTAMINE METHODS IN NORMAL INDIVIDUALS

NO.	NAME	CIRCULATION TIME (RADIUM)			CIRCULATION TIME (HISTAMINE)		DIFFERENCE HISTAMINE CIRC. TIME	DIFFERENCE RADIUM CIRC. TIME
		ARM TO HEART	PUL-MONARY	ARM TO ARM	ARM TO FACE (FLUSH)	ARM TO TONGUE (TASTE)	FLUSH AND ARM TO ARM	TASTE AND ARM TO ARM
		sec.	sec.	sec.	sec.	sec.	sec.	sec.
528	T. C.	4.5	20.0	24.5	22	23	−2.5	−1.5
537	F. T.	5.5	11.0	16.5	20	22	+3.5	+5.0
535	J. K.	4.0	7.0	11.0	15	14	+4.0	+3.0
529	W. G.	6.0	10.0	16.0	21	20	+5.0	+4.0
531	G. McG.	6.0	11.0	17.0	23	21	+6.0	+4.0
524	W. C.	6.0	11.0	17.0	22	—	+5.0	—
536	R. P.	11.0	13.5	24.5	31	31	+6.5	+6.5
530	T. Mc.	4.0	9.5	13.5	20	21	+6.5	+7.5
533	D. L.	3.5	7.5	11.0	19	17	+8.0	+6.0
534	W. S.	3.5	9.0	12.5	21	21	+8.5	+8.5
	Average	5.4	11.4	16.4	21.4	21.1	+5.0	+4.7

in the same solution. The concentration of the histamine was less in these tests than usually used. Both the venous blood flow to the right side of the heart and the pulmonary circulation time were measured with the radioactive deposit method. Table III represents the comparative findings on ten normal subjects. Table IV is the summary of the results obtained on eight patients with cardiovascular disease. In addition to the reaction time of histamine on the facial vessels, both tables include the reaction time on the small vessels of the tongue, as determined by the sensation of metallic taste. The two reaction times of histamine, as a rule, do not differ more than 1 or 2 seconds in normal individuals. The flush may become visible slightly before or after the sensation of taste. As indicated by Tables III and IV, the histamine reaction time is always longer than the arm to arm circulation time. The average arm to arm circulation time in the ten normal individuals was 16.4 seconds, and the average histamine reaction time was 21.4 seconds. The average histamine reaction time, just as observed before,

TABLE IV

COMPARISON OF CIRCULATION TIMES AS DETERMINED BY THE RADIUM AND HISTAMINE METHODS IN CARDIAC PATIENTS

NO.	NAME	AGE	DIAGNOSIS	HEART RATE	ART. PRESS. SYST.	ART. PRESS. DIAST.	VEN. PRESS.	VIT. CAP.	CIRCULATION TIME (RADIUM) ARM TO HEART	CIRCULATION TIME (RADIUM) PULMONARY	CIRCULATION TIME (RADIUM) ARM TO ARM	CIRCULATION TIME (HISTAMINE) ARM TO FACE (FLUSH)	CIRCULATION TIME (HISTAMINE) ARM TO TONGUE (TASTE)	DIFFERENCE HIST. CIRC. TIME FLUSH AND ARM TO ARM	DIFFERENCE RAD. CIRC. TIME TASTE AND ARM TO ARM
		Years		per min.	mm. Hg.	mm. Hg.	mm. H_2O	c.c.	sec.	sec.	sec.	sec.	sec.	sec.	sec.
546	P. M.	66	Myocardial degeneration	56	135	80	–15	2400	–	–	41.0	44	–	+ 3.0	–
547	J. G.	60	Arteriosclerosis	100	138	82	+10	2800	15.0	16.0	31.0	37	39	+ 6.0	+8.0
552	J. W.	55	Myocardial degeneration	80	156	56	+10	3000	12.0	25.5	37.5	44	46	+ 6.5	+8.5
542	E. C.	56	Decompensated hypertension	72	126	82	–	3200	25.0	27.0	5.1	60	–	+ 8.0	–
539	W. N.	42	Auricular fibrillation; Myocardial degeneration	80	130	80	–10	3700	7.0	14.0	21.0	30	–	9.0	–
544	J. S.	65	Myocardial degeneration	70	96	58	–10	2800	7.0	12.0	19.0	31	27	+12.0	+8.0
551	J. G.	62	Myocardial degeneration	100	118	70	+10	1700	13.0	21.0	34.0	47	–	+13.0	–
543	J. J.	68	Arterial hypertension	70	220	108	+20	3700	6.0	14.0	20.0	34	–	+14.0	–
						Average	– – –	– – –	12.1	18.5	31.9	40.9	37.3	+ 9.0	+8.2

is 5 seconds slower than the average arm to arm circulation time. The average arm to arm circulation time of the seven patients with cardiovascular disease was 31.9 seconds; the average histamine reaction time was 40.9 seconds. The histamine reaction time, therefore, was 9 seconds longer than the arm to arm circulation time. This *relatively* greater difference between the two methods in patients with circulatory failure is not unexpected for the histamine reaction time includes the circulation time of the small vessels, in which the velocity of blood flow is proportionately slow. The difference between the histamine and arm to arm circulation times of normal individuals and that of patients with circulatory failure is about the same when the difference is expressed in percentage of the reaction time. The observations suggest that the reaction time of histamine corresponds to the circulation time as closely as under the conditions of observation one may expect. The findings also indicate that the small vessels of the face react very promptly to the action of histamine after it reaches the capillaries. The reaction time of histamine bears such constant relationship to the arm to arm circulation time that the former can be used for the estimation of the velocity of blood flow in man.

After it became established that normal subjects and cardiac patients exhibit a reaction time with histamine which corresponds closely to the circulation time of the same region of the body, we undertook the estimation of the reaction time of patients suffering from various pathological conditions.

The Reaction Time of Histamine in Patients with Cardiovascular Disease.—The patients observed were divided into two groups, according to whether or not they were suffering from symptoms and signs of decompensation at rest at the time of performance of the test. Table V presents some of the findings on patients suffering from cardiovascular disease other than arterial hypertension, without symptoms and signs of congestive failure. Table VI presents the findings on patients with symptoms and signs of congestive failure. In 13 patients suffering from cardiovascular disease without symptoms and signs of circulatory failure, the histamine reaction time varied from 17 to 35 seconds; the average reaction time was 25 seconds. This corresponds to the average circulation time of 24 seconds found with the radioactive test in cardiac patients who showed no symptoms or signs of decompensation at the time when the observations were made.[15, 16] The average vital capacity of 9 patients was 3183 c.c. or 1928 c.c. per meter of body surface. With the exception of patient H. R., the reaction time of all the patients was within normal limits, although the average reaction time was slightly greater than that of the normal individuals studied. This finding is again in harmony with the observations made with the radioactive deposit method, that cardiac patients without symptoms and signs of circulatory failure may have a normal circulation time, and the

TABLE V

THE REACTION TIME OF HISTAMINE IN PATIENTS SUFFERING FROM CARDIOVASCULAR DISEASE, BUT WITH NO EVIDENCE OF CIRCULATORY FAILURE

NAME	AGE	DIAGNOSIS	PULSE	ARTERIAL BLOOD PRESSURE SYSTOLIC	ARTERIAL BLOOD PRESSURE DIASTOLIC	VITAL CAPACITY	VITAL CAPACITY PER SQ. METER	HISTAMINE PH. INJECTION	REACTION TIME
	Years			mm. Hg.	mm. Hg.	c.c.	c.c.	mg. per Kg.	seconds
T. C.	14	Rheumatic heart disease; Mitral stenosis	88	120	56	3800	2400	0.0011	17
B. N.	34	Myocardial degeneration; Auricular fibrillation	56	140	70	–	–	0.0010	20
E. S.	15	Rheumatic heart disease; Auricular fibrillation	92	110	50	–	–	0.0008	20
J. W.	55	Syphilitic heart disease; Aortitis and aortic insufficiency	84	140	52	3450	1875	0.0012	21
J. W.	55	Syphilitic heart disease; Aortic insufficiency	84	140	52	3450	–	0.0010	22
I. M.	32	Rheumatic heart disease; Mitral stenosis and insufficiency	76	140	92	–	1895	0.0012	21
I. R.	21	Rheumatic heart disease; Aortic insufficiency and mitral stenosis	72	122	44	3800	2290	0.0011	25
M. C.	23	Rheumatic heart disease; Mitral stenosis and insufficiency	72	126	74	2750	1870	0.0011	25
C. D.	48	Rheumatic heart disease; Auricular fibrillation	68	130	72	4100	2350	0.0013	26
A. C.	20	Acute rheumatic fever; Mitral stenosis	92	–	–	3000	2200	0.0011	26
E. T.	60	Arteriosclerosis; Myocardial degeneration	72	140	90	2550	1510	0.0011	29
A. W.	72	Arteriosclerosis; Myocardial degeneration	82	154	76	–	–	0.0011	30
D. S.	58	Arteriosclerosis; Myocardial degeneration	72	156	100	1800	948	0.0012	30
H. R.	62	Myocardial degeneration; Auricular fibrillation	72	128	60	3400	1910	0.0012	35

vital capacity of these patients may be slightly reduced.[15] Three of the four patients who showed fibrillation of the auricles showed reaction times within normal limits. This finding indicates, as observed before, that the velocity of blood flow may be normal with total irregularity of the heart beat if the function of the myocardium is good. Patient C. D. was an intelligent window washer who served in the Spanish-American War in 1898 and was then diagnosed as suffering from completely irregular pulse. After having a cardiac irregularity for over 30 years he walks with ease up 14 flights of stairs without stopping. He was admitted to the hospital on account of a minor surgical condition. The general reaction of these patients to histamine was the same as that of normal subjects. Only one of the patients complained of severe headache which lasted 10 minutes.

The reaction time of histamine in patients with symptoms and signs of congestive failure at time of test varied from 21 to 82 seconds. The average reaction time was 47 seconds. The average arm to arm circulation time of similar patients observed with the radioactive deposit method was 38 seconds. The average difference between the histamine reaction time of normal subjects and that of patients with circulatory failure was approximately 100 per cent. The same difference was found with the radioactive deposit method. The average vital capacity of patients was 1807 c.c., or 1007 c.c. when reduced to the value for a square meter of body surface. This average vital capacity was lower than that of patients with signs of circulatory failure in whom the circulation time was measured with the radioactive deposit method.

The lower vital capacity is due partly to the fact that a relatively larger number of patients observed by the histamine method suffered from severe congestive failure than those observed before with the radioactive deposit method. This is also indicated by the fact that eleven out of the twenty-six patients died, in spite of treatment, within three months after the performance of the test. The average reaction time of the 11 patients who died in the hospital as a result of circulatory failure was 50 seconds. This average reaction time of the patients who died from circulatory failure was not appreciably longer than that of patients who improved, or whose condition remained unaltered. We, therefore, did not observe a critical reaction time with prognostic significance. As indicated in Table VI, the prolongation of the reaction time was not necessarily proportional to the severity of the clinical condition, though a markedly prolonged circulation time was always associated with severe circulatory failure. It is of special interest in connection with this statement that patient M. L., on whom repeated tests were performed 8 hours before his death, had a reaction time of only 28 and 29 seconds. This patient was suffering from syphilitic heart disease and paroxysmal dyspnea (cardiac asthma) of one month's duration. He was admitted to the hospital 24 hours before his death

TABLE VI

THE HISTAMINE REACTION TIME IN PATIENTS WITH CIRCULATORY FAILURE

NAME	AGE	HEART RATE	ARTERIAL BLOOD PRESSURE SYSTOLIC	ARTERIAL BLOOD PRESSURE DIASTOLIC	VITAL CAPACITY	VITAL CAPACITY PER SQ. METER	HISTAMINE PH INJECTION	REACTION TIME	DIAGNOSIS AND REMARKS
	(Years)	per min.	mm. Hg.	mm. Hg.	c.c.	c.c.	mg. per Kg.	seconds	
M. L.	45	104	170	50	–	–	0.0009	28	Syphilitic heart disease with aortic insufficiency. Died as result of pulmonary edema 8 hours later.
M. L.	45	100	164	48	–	–	0.0009	29	
J. M.	44	150	–	–	1000	525	0.0009	33	Myocardial degeneration; auricular fibrillation; anasarca.
J. R.	61	70	145	95	2800	1400	0.0008	34	Coronary sclerosis and cardiac infarct five months previously. Weakness, no edema or other signs of congestive failure.
J. R.	61	70	145	90	2800	1400	0.0006	45	
G. M.	60	92	208	106	1650	970	0.0010	35	Myocardial degeneration; arterial hypertension; dyspnea; slight dependent edema.
C. H. S.	±60	108	160	114	–	–	0.0012	35	Myocardial degeneration; auricular fibrillation; dyspnea.
W. M.	65	68	160	60	1800	975	0.0011	35	Myocardial degeneration; arteriosclerosis; moderate dependent edema; Cheyne-Stokes breathing.
R. C.	65	60	126	65	1700	870	0.0010	35	Myocardial degeneration; arteriosclerosis; auricular fibrillation; dyspnea; emphysema.
R. C.	65	60	118	60	1700	870	0.0008	38	
J. W.	55	112	163	60	2650	1160	0.0009	36	Syphilitic heart disease; aortic insufficiency; orthopnea; dependent edema.
B. O'L.	75	96	190	130	1500	800	0.0009	37	Arteriosclerosis; myocardial insufficiency; orthopnea; dependent edema.
B. O'L.	75	92	190	130	1500	800	0.0009	40	
W. W.	64	64	170	80	2900	1810	0.0011	37	Myocardial degeneration; moderate dyspnea.
C. H. S.	±60	100	–	–	1800	1130	0.0011	42	Myocardial degeneration; arteriosclerosis; Cheyne-Stokes breathing.
C. H. S.	±60	100	156	124	1800	1130	0.0011	59	
T. W.	75	60	–	–	2700	1380	0.0011	43	Myocardial degeneration; arteriosclerosis; emphysema; dyspnea; dependent edema.

TABLE VI—CONT'D

NAME	AGE	HEART RATE	ARTERIAL BLOOD PRESSURE SYSTOLIC	DIASTOLIC	VITAL CAPACITY	VITAL CAPACITY PER SQ. METER	HISTAMINE PH INJECTION	REACTION TIME	DIAGNOSIS AND REMARKS
	(Years)	per min.	mm. Hg.	mm. Hg.	c.c.	c.c.	mg. per Kg.	seconds	
M. J.	75	110	–	–	–	–	0.0005	45	Myocardial degeneration; auricular fibrillation; emphysema; dyspnea; slight dependent edema.
M. J.	75	–	–	–	–	–	0.0008	49	
J. B.	47	48	204	114	1350	740	0.0011	45	Syphilitic heart disease; aortic insufficiency; arterial hypertension; orthopnea; marked dependent edema.
D. P.	61	110	–	–	1800	1020	0.0008	49	Myocardial degeneration; auricular fibrillation; orthopnea; edema.
P. D. M.	68	76	220	112	2150	1180	0.0008	49	Myocardial degeneration; arterial hypertension; orthopnea; dependent edema.
F. G.	74	96	216	106	1000	575	0.0010	50	Myocardial degeneration; emphysema, dyspnea; edema; arterial hypertension.
D. McN.	56	68	116	84	2000	1040	0.0011	50	Myocardial degeneration; auricular fibrillation; cardiac paroxysmal dyspnea; orthopnea.
D. McN.	56	76	110	84	2000	1040	0.0008	62	
D. McN.	56	68	108	86	2000	1040	0.0006	82	
W. P.	55	64	–	–	1300	690	0.0009	53	Rheumatic heart disease; auricular fibrillation; anasarca.
W. P.	55	62	–	–	1300	690	0.0009	55	
T. V.	69	74	152	90	1050	525	0.0010	56	Myocardial degeneration; orthopnea; edema.
D. McN.	56				2200	1150	0.0008	57	Myocardial degeneration; auricular fibrillation; cardiac paroxysmal dyspnea; orthopnea.
D. McN.	56				2200	1150	0.0006	58	
D. McN.	56	72	114	92	2200	1150	0.0011	64	
A. L. P.	75	80	178	60	800	480	0.0013	57	Aortic insufficiency; anasarca; syphilitic heart disease.
A. L. P.	75	84	162	58	–	–	0.0013	58	
D. R.	66	76	130	42	1600	850	0.0010	60	Syphilitic heart disease; aortic insufficiency; dyspnea, anasarca.
C. H. S.	±60	–	–	–	–	–	0.0012	67	Myocardial degeneration.
C. H. S.	±60	108	–	–	–	–	0.0012	70	

with symptoms and signs of acute pulmonary edema. Prompt venesection and strophanthin intravenously improved the patient's condition, and he felt comfortable. The next day he suffered from a similar attack, from which, despite treatment, he did not recover. Postmortem examination revealed syphilitic aortitis with aortic insufficiency, vegetative endocarditis, right hydrothorax, pulmonary edema and ascites. The clinical behavior and autopsy findings in this patient indicated that the death was due to sudden failure of the left side of the heart. It is suspected clinically that a slight disproportion between the function of the two sides of the heart may be of grave consequence. It is obvious that in such a type of failure, the velocity of blood flow is not necessarily prolonged, and in the explanation of the death other factors than change in velocity must play more important rôles. In patients with myocardial degeneration the prolongation of circulation time is more apt to be proportionate to the severity of clinical condition than in patients with valvular disease. This is illustrated by patient C. H. S., who, as his condition grew worse, exhibited a continually increasing reaction time (35, 42, 59, 67, 70 seconds).

It was noted during these observations that several patients with signs of congestive failure exhibited more marked unpleasant reactions to the injections of histamine than normal subjects or patients without symptoms and signs of congestive failure. In patients with circulatory failure following the injection of histamine the flush was often more intense and of longer duration than in normal subjects. This prolonged and marked flush was especially intense in patients who, in addition to the myocardial degeneration, exhibited clinical evidence of emphysema of the senile type. In patient T. W., for example, who had shown definite evidence of emphysema including an inspiratory restriction of the lower ribs (Hoover's sign), there was a flush of the face which lasted for 6 minutes following the intravenous injection of 0.001 mg. of histamine per kg. We have never observed in normal subjects a flush of such long duration following a single similar intravenous dose. It is of great interest that 10 of the patients of this group, in contrast to normal subjects and to the other group of patients with cardiovascular disease, without evidence of decompensation, developed dyspnea of 2 to 3 minutes' duration. The type of dyspnea varied. In some of the patients it was predominantly expiratory and wheezing. Three patients, prior to the administration of histamine, showed a low diaphragm which moved but slightly under the fluoroscope, and an inspiratory restriction of the lower ribs (Hoover's sign). After histamine they developed a temporarily accentuated Hoover's sign. We are unable to state with certainty whether the restriction of the diaphragm was the result of associated emphysema or whether it was caused by the dyspnea as a result of the circulatory failure, for we believe that an inspiratory restriction of the lower ribs can be caused

by other types of dyspnea than that due to emphysema. Several of the patients who developed dyspnea of short duration after histamine have shown no evidence of emphysema, but they have suffered previously from paroxysmal nocturnal dyspnea (cardiac asthma). One of the patients who showed the most marked reaction following the administration of histamine was a young man (R. R.) 30 years old, who was suffering from rheumatic heart disease with signs of aortic insufficiency and mitral stenosis. He was given an intravenous injection of 0.0008 mg. of histamine phosphate per kg. About 14 to 20 seconds after injection there was a gradually increasing dyspnea, and the patient had to sit up. There was both inspiratory and expiratory difficulty. The dyspnea lasted for 5 minutes. When 0.2 c.c. of epinephrin of 1:3000 was given by vein, the patient received instant relief. The vital capacity changed from 3500 c.c. to 1500 c.c. even shortly after the dyspnea was relieved. The lowered vital capacity gradually became normal after the administration of adrenalin. It is of interest that this patient was readmitted two months later because of severe attacks of nocturnal dyspnea. This patient showed an increased sensitivity to histamine. Histamine in this and in other cardiac patients produced dyspnea similar to that observed in patients with acute bronchitis, asthma and pulmonary emphysema. That dyspnea in these patients with cardiovascular disease was not due to peripheral dilatation of the vessels is shown by the fact that the change in blood pressure was not more marked than in other patients without dyspnea. But the most weighty evidence against the dyspnea being of peripheral origin is the observation that in a number of patients the dyspnea started at about the half period of the histamine reaction time. In these patients it is probable that the dyspnea was due to sensitivity of the pulmonary structures to histamine. The fact that adrenalin relieved the dyspnea favors the conception that the dyspnea in these cases was due to the sensitivity of the smooth muscles of the bronchioles to histamine. Whether in other patients in whom the dyspnea started after the elapse of the reaction time, peripheral dilatation of the coronary or other vessels played a rôle cannot be stated with any certainty. The test should not be applied in patients with evidence of coronary disease. In order to avoid unpleasant reactions in patients with myocardial degeneration and dyspnea small doses of 0.005 mg. were given first and only when no reaction to such a dose was noted was the amount increased.

The Histamine Reaction Time in Patients With Arterial Hypertension.—This group of patients, with the exception of patients I. M. and S. Z., were ambulatory and were living a normal life. With the exception of these two patients all had subjective complaints only. All the ambulatory patients showed reaction times which were within the limits of normal. The two patients who exhibited a prolonged reaction time were hospitalized, and in addition to the hypertension they exhib-

ited symptoms and signs of marked cardiovascular changes. The findings presented in Table VII are again in harmony with the observations made before,[16] that the velocity of blood flow is within the limits of normal or slightly prolonged in patients with arterial hypertension but without circulatory failure. The average blood pressure was 187/118 mm. The average circulation time was 26 seconds. The average circulation time of the nine patients who were ambulatory and able to attend work was 23 seconds, which is the average circulation time observed in normal subjects.

The Histamine Reaction Time in Patients With Pulmonary Emphysema.—The six patients studied in this group suffered from such severe weakness and dyspnea that they were confined to bed. Chronic bronchitis and attacks of bronchial asthma were etiological factors in the production of the emphysema. The severity of the respiratory disturbance was so marked that four of the patients have shown marked cyanosis over the face and mucous membranes. All patients exhibited, in addition to the signs described in Table VIII, a low diaphragm with slight excursion, hyperresonant percussion notes, obliteration of the cardiac dullness, and numerous rhonchi and râles. As indicated in Table VIII, the reaction times were well within the limits of normal, with the exception of patient Th. W. The average reaction time was 26.4, slightly above the average of normal reaction times. If we exclude the last patient, who showed marked prolongation in the blood flow, the average reaction time is 24 seconds. In these patients with

TABLE VII

THE HISTAMINE REACTION TIME OF PATIENTS WITH ARTERIAL HYPERTENSION

NAME	AGE	HEART RATE	ARTERIAL BLOOD PRESSURE SYSTOLIC	ARTERIAL BLOOD PRESSURE DIASTOLIC	HISTAMINE INJECTED	REACTION TIME
	Years	per min.	mm. Hg.	mm. Hg.	mg. per Kg.	seconds
S. M.	40	76	174	110	0.0006	17
V. H.	45	100	210	130	0.0005	19
F. L.	50	88	188	114	0.0009	20
F. G.	35	96	170	104	0.0006	20
F. G.	35	96	164	104	0.0004	26
B. L.	59	84	190	130	0.0010	21
J. G.	56	104	210	138	0.0012	21
J. G.	56	108	210	140	0.0010	22
J. G.	56	108	190	132	0.0012	22
J. G.	56	104	168	126	0.0012	23
J. G.	56	92	150	108	0.0012	24
H. D.	65	80	194	108	0.0011	26
H. D.	65	84	182	100	0.0006	26
M. F.	64	96	190	98	0.0011	26
M. F.	64	96	206	100	0.0008	31
A. T.	41	84	215	125	0.0010	28
A. T.	41	80	225	135	0.0010	30
J. M.	60	80	–	–	0.0011	36
S. X.	71	104	180	120	0.0006	40

TABLE VIII

THE HISTAMINE REACTION TIME IN PATIENTS WITH MARKED PULMONARY EMPHYSEMA

NAME	AGE	HEART RATE	VITAL CAPACITY	VITAL CAPACITY PER SQ. METER	HISTAMINE MG. PER KG.	REACTION TIME	REMARKS
	Years	per min.	c.c.	c.c.		seconds	
P. R.	± 65	78	2000	1038	0.0012	18	Cough and attacks of asthma for 17 years. Marked dyspnea. Unable to walk but few steps. Marked cyanosis. Positive Hoover's and other signs of emphysema.
P. R.	± 65	76	2000	1038	0.0008	24	
J. H.	53	100	1350	798	0.0009	24	Chronic cough for 30 years. Marked dyspnea with cyanosis. Unable to work. Able to walk on level but slowly. Physical signs of emphysema.
M. G.	63	70	3100	1480	0.0010	24	Chronic cough and productive expectoration for 20 years. Shortness of breath at slightest exertion. Comfortable at rest. Cyanosis, barrel-shaped chest and other signs of emphysema. Severe arteriosclerosis. Auricular fibrillation.
M. G.	63	68	3100	1480	0.0007	26	
C. W.	66	60	1125	635	0.0006	25	Chronic cough and frequent attacks of asthma for 17 years. Cyanosis and other signs of emphysema.
C. W.	66	64	1200	640	0.0006	23	
E. B.	74	90	1100	749	0.0007	27	Cough and dyspnea of many years duration. Unable to walk but short distance. Clinical signs of emphysema and of arterial hypertension.
Th. W.	75	60	—	—	0.0010	13	Cough of years duration. Dyspnea, signs of emphysema, including Hoover's sign.
Th. W.	75	60	2700	1380	0.0006	—	

pulmonary emphysema, therefore, although the vital capacities per square meter of body surface were approximately the same as those of patients with extreme severe circulatory failure, the velocity of blood flow was within normal limits. The physical disability in these patients was due, therefore, primarily to the failure of the respiratory function of the lungs. In emphysema with complete disability, the velocity of blood flow through the lungs, as observed before, may be normal. In some instances decrease in the velocity of blood flow may occur if there is also cardiac failure. The significance of the normal velocity of blood flow in patients with pulmonary emphysema was pointed out in a previous communication.[17]

All patients with emphysema, bronchitis and bronchial asthma showed temporarily increased dyspnea with the appearance of symptoms and signs of bronchial asthma after the administration of histamine. The dyspnea was transient. It was also noted that patients with emphysema exhibited an unusually prolonged facial flush.

The Histamine Reaction Time in Patients With Clinical Evidence of Hyperthyroidism.—The rapid heart rate, the warm skin, the results of direct capillary observation, the high basal metabolism, all suggest that the velocity of blood flow is rapid in patients with increased thyroid secretion. Liljestrand and Stenström[18] found an increased minute volume output of the heart in patients suffering from hyperthyroidism. Table IX presents a correlation between the pulse rate and the rate of

TABLE IX

THE HISTAMINE REACTION TIME IN PATIENTS WITH HYPERTHYROIDISM

NAME	AGE	HEART RATE PER MIN.	REACTION TIME
	Years		Seconds
M. C.	23	104	9
E. B.	32	124	9
J. H.	36	120	11
J. H.	36	134	12
W. F.	38	94	No reaction
W. F.	38	—	15
W. F.	38	—	16
W. F.	38	79	15
J. H.	36	132	19
J. H.	36	128	22
D. H.	54	108	24
D. H.	54	108	27

the metabolism and histamine reaction time. As expected, the velocity of blood flow was increased in all the patients except in patient D. H. The average reaction time was 16.3 seconds, which is 29 per cent lower than the average circulation time of 23 seconds in normal subjects. The increased velocity of 29 per cent corresponds closely to the average rise of 35 per cent in the basal metabolism. A correlation between the increase in cardiac rate, basal metabolism, and reaction time was not present in a given patient.

The duration of flush was short. Otherwise, the reaction of the patients to histamine was the same as that of normal subjects.

The Histamine Reaction Time in Patients With Pernicious Anemia.—It was expected that the determination of the histamine reaction time by the appearance of the flush might be difficult in patients with marked anemia. It was found that several patients with a severe degree of primary anemia showed no definite flush from histamine. Several of these patients could indicate the reaction time from the sudden appearance of metallic taste in the tongue. We could not establish a definite level of hemoglobin or red cell count below which the flush cannot be determined, and it is possible that the reaction of the capillaries and other small vessels may be altered in pernicious anemia. This possibility is suggested by the fact that at times the appearance of slight facial flush may be the earliest indication of the approaching remission, and it may appear without any increase, or even with a decrease, in the hemoglobin or red cell content of the blood.

Seven patients, in whom we succeeded in determining the histamine reaction time, both by flush and by the appearance of taste in the tongue, are presented in Table X. The average hemoglobin content of

TABLE X

THE REACTION TIME IN PATIENTS WITH PERNICIOUS ANEMIA

NAME	AGE	HEART RATE PER MIN.	RED BLOOD CELLS IN MILLIONS	REACTION TIME
	Years			Seconds
S. L.	58	104	2.40	9
J. F.	53	84	—	10
F. N.	64	68	3.20	10
M. A.	55	92	1.34	11
H. O'N.	70	84	3.46	15
K. M.	60	96	1.19	16
P. C.	63	80	1.79	10

the blood was 38 per cent, that of the red cell content 2.23 millions, and the average reaction time 11.5 seconds. The average velocity of blood flow was twice as rapid as in normal individuals. The increase in velocity of blood flow is proportional to the decrease of red cell count and hemoglobin.

The Histamine Reaction Time of the Human Brain Vessels.—The circulation time of different parts of the body may be different. In animals the circulation time of different organs was measured by G. N. Stewart.[19] In man it was shown by us that the circulation time of the small vessels of the upper arm and elbow is approximately the same as that of the face and tongue. During a study of the effect of histamine on the small vessels of the human body,[9a] it was observed that following the sudden intravenous injection of small amounts of histamine the intraspinal pressure showed a sudden rise which lasted between 1 and

3 minutes. In two patients suffering from brain tumor it was also observed during operative exposure of the brain that 0.001 mg. per kg. of histamine caused a flushing of the surface of the brain. With the onset of this flush the volume of the brain showed slight increase and a marked increase in the pulsation. All of these changes lasted about 90 seconds. From these and other observations previously reported, it was considered that the small vessels of the brain were very sensitive to histamine. The period which elapsed between the injection and onset of a rise of pressure indicated at once that this must correspond to the circulation time from the arm to the brain. In a group of patients suffering from various neurological conditions, in whom the performance of spinal fluid pressure determination was necessary from a diagnostic or therapeutic point of view, a small dose of histamine (0.001 mg. per kg. or less) was injected. A small glass manometer was connected with the spinal needle, and the movement of onset of the rise in spinal pressure was determined. (It is essential that fluid should not be lost previously to the injection of histamine.) The time of onset of the rise was then compared with the time of the onset of flush which was noted by another observer. Table XI shows the findings in subjects in whom the histamine reaction time from the right elbow to the face and to the brain respectively was measured simulta-

TABLE XI

COMPARISON OF THE HISTAMINE REACTION TIME FROM ARM TO FACE AND ARM TO BRAIN

NAME	AGE	DIAGNOSIS	HEART RATE PER MIN.	BLOOD PRESSURE SYSTOLIC	BLOOD PRESSURE DIASTOLIC	ARM TO FACE REACTION TIME	ARM TO BRAIN REACTION TIME
	Years			mm. Hg.	mm. Hg.	Seconds	Seconds
P. D.	19	Epilepsy	110	114	84	13	12
M. Cr.	22	Syphilis	112	110	84	15	15
R. S.	57	Cervical rib	84	100	64	17	16
E. S.	53	Alcoholic neuritis	80	140	90	16	17
			84	132	88	19	18
C. K.	18	Multiple sclerosis	90	120	65	19	17
O. B.	24	Epilepsy	68	108	78	18	19
N. J.	52	Epilepsy	100	120	90	20	20
			90	116	78	18	19
C. L.	53	Syphilis	76	136	76	21	21
R. B.	30	Chronic enceptalitis	80	126	80	26	26

neously. In the patients presented in Table XI, as well as in many others, it was striking to observe how closely the reaction time of the face and vessels of the brain corresponded. The maximum difference was not more than two seconds. The average reaction time of the brain and that of the face of the same individual under identical conditions was 18 seconds. From the foregoing it is evident that the circulation times of the brain and of the face are identical. The average reaction

time in these patients was shorter than that of those included in Table I. The difference is probably due to the fact that the patients were excited as a result of the performance of spinal puncture.

An Attempt to Estimate the Velocity of the Arterial and Venous Blood Flow Separately.—An attempt was made to estimate the arterial and the venous portions of the circulation between the elbow and face by determining the histamine reaction time of normal subjects and allowing the same individuals to inhale deeply and rapidly a single breathful of amyl nitrite vapor through a small rubber cone. The time between the end of the inhalation and the appearance of flush should correspond to the time necessary for a particle of blood to travel from the pulmonary capillary through the pulmonary artery and through the arteries after leaving the heart. The distance of these arterial vessels corresponds to the distance travelled from the elbow to the capillaries through the venous vessels. It was found, however, that a number of subjects do not respond with as marked and easily recognizable a flush to amyl nitrite as they do to histamine. In the few subjects in whom definite reactions were obtained, the time was about half of that obtained with histamine, and about the same as reported by Bornstein[12] following the inhalation of carbon dioxide. Assuming that the diffusion of amyl nitrite is instantaneous through the pulmonary capillaries, it would follow that the circulation time of the arterial (pulmonary vein and peripheral arteries) and venous portions (peripheral vein and pulmonary artery) is about the same. In analogy with the knowledge of the relative diameters of the aorta and vena cava and the respective velocity of blood flow in them it would follow that in the pulmonary vein the blood flow velocity must be twice as slow as in the pulmonary artery. As the reaction to amyl nitrite was not definite in a larger number of subjects, the problem was not considered as settled.

DISCUSSION

In outlining the problem of this investigation it was stated that in order to be applicable to man, the histamine method should fulfill a number of requirements. In light of our experience histamine fulfills these prerequisites in the following way:

1. During observations on over 200 patients, no serious effects were observed. In a number of patients who suffered from circulatory failure with emphysema, bronchial asthma and bronchitis, attacks of dyspnea were precipitated. It was observed that the respiratory mechanisms of these patients were hypersensitive to the effect of histamine, and, therefore, in later observations the first dose injected was half of the usual dose. Only if unpleasant side effects were not observed after the small dose, was the second, larger, dose administered. Several of the patients studied complained of pulsating headache and a sensation of weakness of a few minutes' duration.

2. Histamine does not influence appreciably the velocity of blood flow during the first circuit of the blood, following the injection. This is supported by the finding that the acceleration of the pulse starts just before or after the appearance of the flush. That histamine does not increase the velocity of blood flow before the appearance of flush is supported by the finding that the histamine reaction time is slightly longer than the circulation time.

3. Repeated tests on the same person, as well as disappearance of the histamine effect, indicate that its effect in the body lasts but a short time, and therefore the test can be repeated at short intervals.

4. The close correspondence between the circulation time and the histamine reaction time also indicates that the minute vessels dilate promptly after the arrival of the histamine.

5. The appearance of the flush is definite enough to make it possible to estimate the circulation time of normal subjects, and patients with varied pathological conditions.

Comparing our experiences with the histamine, the radioactive, and the dye methods for the estimation of the velocity of blood flow in man, we feel that the histamine method offers certain advantages, especially in so far as its use in the clinic is concerned, over the other methods. The advantages of the histamine method over the radioactive deposit method are as follows:

1. Its use is simple, requiring no complicated apparatus and technic. With slight skill it can be performed by anybody with the aid of a stop watch.

2. The expense of the test is minimal, and histamine is easily available.

3. The test can be repeated every five to ten minutes, while the radioactive method, on account of the persistence of activity, can be repeated only at three-hour intervals.

4. The test can be performed at the bedside, while in the radioactive method the patient has to be moved to the instrument.

The disadvantages of the method as compared with the radioactive method are as follows:

1. The radioactive method is objective and more exact. It makes possible the measurement of the velocity of blood flow of several areas of the body simultaneously, including important circulatory areas (pulmonary circuit), the circulation time of which cannot be measured with histamine.

2. Short unpleasant reactions observed occasionally after the administration of histamine are not present after the intravenous administration of radioactive deposit.

3. In colored and anemic people the histamine test cannot be applied.

In comparing the histamine method with the dye methods, we feel that the histamine method is more exact, the technic simpler and less

disturbing to the patient. Furthermore, it can be performed by one person.

The use of the intravenous administration of histamine for the estimation of the velocity of blood flow serves a useful clinical purpose if it is applied with care and the results are interpreted with proper critique. The variation of the results is not greater than may be expected from the best biological methods which are influenced by similar variables. Much significance should not be attached to slight variations in the circulation time of the same or of different patients. Marked variations in the circulation time are of special practical significance in the differentiation of myocardial insufficiency from emphysema, on the one hand, and circulatory insufficiency from nephritis with edema, on the other. In such patients the estimation of the

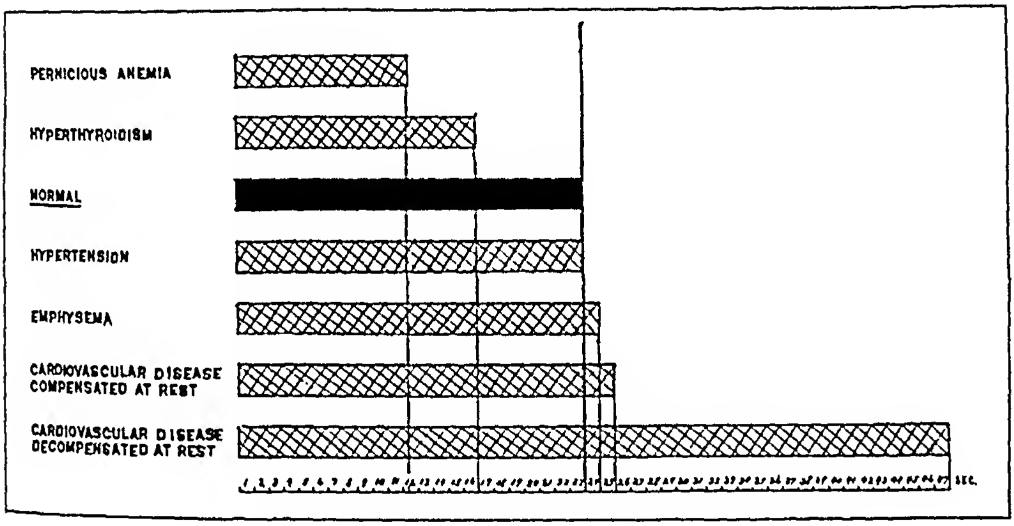

Fig. 1.—The histamine reaction time in health and in disease.

velocity of blood flow with histamine is a useful aid in the clinical evaluation of the condition.

In addition to the vessels of the face, it has been shown that the vessels of the human brain are sensitive to the action of histamine. As a result of the intravenous injection of histamine, flushing of the surface of the brain due to dilatation of the minute vessels occurs. Coincident with this flush there is a swelling and increased pulsation of the brain, and the cerebrospinal fluid pressure shows a steep rise. The rise reaches its maximum within 15 to 40 seconds, and similarly to the facial flush, reaches the normal level within three minutes. A very close relationship has been found between the time of onset of the flush and the rise in intracranial pressure. The procedure, therefore, makes it possible for the first time to estimate the velocity of blood flow from an arbitrarily chosen point to the small vessels of the brain.

An attempt was made to separate the circulation time of the venous and arterial blood from elbow to face. The amyl nitrite inhalation, as

well as the observation of Bornstein with CO_2 inhalation, indicates that the time from the capillaries of the lung to the face is about the same, or slightly less than that from the elbow to the pulmonary capillaries. As anatomical and physiological considerations indicate that the velocity in the large peripheral veins is about half that of the large peripheral arteries, it follows that the velocity of the blood flow in the pulmonary artery is also about twice that of the vein. It was observed previously that average circulation time of the peripheral venous flow is 6.7 seconds; the pulmonary circulation time 6.5 seconds; the actual loss of time in the heart is 1 to 2 seconds; the arm to arm arterial circulation time is 18 seconds; the arm to capillary circulation time is 23 seconds. It follows from these data, that the capillary circulation time is 5 seconds, the circulation time of the pulmonary artery 2.1 seconds, and that of the pulmonary vein 4.2 seconds.

The average prolongation of the velocity of blood flow in patients with symptoms and signs of circulatory failure was about 100 per cent above the average normal velocity. A number of patients with severe myocardial failure have shown a prolongation of over 200 per cent above the average normal circulation time. While in patients with myocardial failure without valvular damage the more prolonged circulation time was associated with severe circulatory failure, no definite prognostic value can be attached to the circulation time. The average circulation time of 11 patients who died as a result of severe circulatory failure was not markedly different from that of the other group of 15 patients who either recovered or were unimproved three months after the test. Occasionally severe derangement of the circulation may be present with normal or only slightly prolonged circulation time. Such a condition may exist when slight disproportion between the function of the two sides of the heart is present, a condition which occurs probably more frequently than is now recognized. In luetic aortic insufficiency the myocardium of the left ventricle may fail functionally as a result of fatigue, while the intact musculature of the right chambers continues to throw blood into the lung. That such a condition may soon lead to serious consequences is evident.

The fact that circulation time may be of value in differentiating ventilatory and circulatory insufficiency, is of great significance, for the two conditions have many common characteristics, and they offer great differential diagnostic difficulty. This difficulty becomes even greater because pulmonary emphysema and circulatory failure may often be present in the same individual. In such patients the simultaneous measurements of several characteristics of the circulation, such as of the vital capacity, circulation time and venous pressure, will be a useful aid in the estimation of the two conditions.

Patients with hyperthyroidism and severe primary anemia have shown considerable increase in the velocity of blood flow. The increase

was especially marked in patients with pernicious anemia. In patients with hyperthyroidism no definite relationship was observed by this method in the individual cases between the velocity of blood flow and the rise in basal metabolism.

We attach significance to the observation that small amounts of histamine may precipitate an attack of dyspnea of short duration in patients with bronchitis, bronchial asthma, and emphysema, as well as in certain patients with severe myocardial failure who suffer from typical attacks of cardiac asthma. The observation of the identical reaction in patients suffering from two diseases suggests that the mechanism of paroxysmal cardiac dyspnea, at least in one group of cardiac patients, may be similar to the dyspnea of bronchial asthma in which it is recognized that the bronchial musculature is sensitive to histamine. The suspicion that in a group of people with myocardial damage the changed state of the bronchial muscles, or the disturbed mechanism of the histamine plays a rôle in the precipitation of attacks of dyspnea may be understood in the light of recent knowledge on the fate and rôle of histamine in the body.[20]

SUMMARY AND CONCLUSIONS

1. The intravenous administration of histamine phosphate in amounts of 0.001 mg. or less per kg. of body weight in solution of 1:5000, or 1:10,000, causes a dilatation of the minute vessels of the face and of the brain with regularity.

2. The reaction time of histamine between the site of intravenous injection and the vessels of the face and brain can be estimated with an average variation of two seconds.

3. Estimation of the histamine reaction time in normal subjects and in patients with various pathological conditions simultaneously with determination of the circulation time by the radioactive method indicates that the histamine reaction time is a measure of the velocity of blood flow.

4. The observations reported in this study confirm the conclusions previously expressed on the significance of the circulation time in health and disease, as measured by the radioactive method.

5. In 65 normal subjects the histamine reaction time varied between 13 and 30 seconds, the average reaction time being 23 seconds between the antecubital vein and the small vessels of the face.

6. In 11 normal subjects the histamine reaction time between the cubital vein and the small vessels of the brain varied between 12 seconds and 26 seconds, the average reaction time being 18 seconds.

7. (a) It was again observed that in compensated cardiac patients the velocity of the blood flow may be within limits of normal, while in patients with symptoms and signs of circulatory failure a prolongation of over 200 per cent may be present.

(b) In patients with circulatory failure the circulation time varied between 21 and 82 seconds, with an average of 47 seconds.

(c) The average histamine reaction time of 11 patients who as a result of circulatory failure died within 3 months following the test was 50 seconds, as contrasted with 45 seconds, the average reaction time of patients with severe circulatory decompensation who either improved or showed no change within three months after the test.

(d) In failure of the left ventricle associated with pulmonary edema, such as occurs in diseases of the aorta, signs of severe circulatory failure may be present with normal or only slightly prolonged circulation time.

(e) In a group of patients with cardiovascular disease but with no symptoms and signs of circulatory failure at rest and moderate exercise, the velocity of blood flow was normal, but the vital capacity was slightly reduced. This fall in the vital capacity before the slowing of the velocity of blood flow, confirms the conception expressed before, that in progressive circulatory failure the pulmonary vascular bed may show change before there is a detectable change in the velocity of blood flow, and that the slowing of the velocity of blood flow precedes the rise in the venous pressure. During progressive improvement of the circulation the change in these characteristics of the circulation is reversed.

8. A markedly prolonged circulation time was always associated with severe circulatory failure, but the reverse was not always true. Changes in the velocity of blood flow do not necessarily have prognostic significance.

9. It was shown again that the velocity of blood flow in patients with essential arterial hypertension, but without circulatory failure, and in emphysema, is normal.

10. In anemia and hyperthyroidism the velocity of blood flow is considerably increased. The average velocity in a group of patients with hyperthyroidism was proportionate with the average increase in basal metabolism, but a similar relationship in individual cases was not always observed.

11. Among the pathological conditions studied, the velocity of the blood flow was most increased in pernicious anemia (double of the normal rate), and the decrease was greatest in severe circulatory failure (half of the normal rate). The difference between the velocity of blood flow in a given case of pernicious anemia and a severe circulatory failure was ninefold.

12. Patients with bronchitis, bronchial asthma, pulmonary emphysema and severe myocardial failure may show temporary dyspnea associated with signs of bronchial spasm following the intravenous administration of histamine. In these cases the test should be applied cautiously; half of the dose (0.0005 mg. per kg.) should be given intra-

venously slowly (5 seconds) as a test dose before the usually applied dose is given.

13. The measurement of the velocity of blood flow is an important diagnostic aid in differentiating certain diseases associated with dyspnea and edema (circulatory failure and respiratory failure; nephritis and circulatory failure).

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DISTORTION OF THE BRONCHI BY LEFT AURICULAR ENLARGEMENT*

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THE effects of the enlargement of the left auricle on the structures of the mediastinum, which follow upon long-standing mitral disease have been known for a long time, and have been repeatedly demonstrated; but the value of detailed x-ray and fluoroscopic study in all cases suggestive of mitral disease does not seem sufficiently well realized. There are three separate items worthy of investigation: the study of the outline of the enlarged chamber itself, the study of esophageal displacement, and the study of bronchial displacement.

The anatomical localization of the left auricle and its proper relationship to other structures within the chest is the most important factor in the explanation of the phenomena following its enlargement. Jaffe[1] and Groedel[2] have investigated the position of the auricle by x-rays and anatomical dissection, and Stoerk[3] has reviewed the anatomy in the cadaver, bringing forward new points and emphasizing the important features of the relation of the bronchi and esophagus to the left auricle.

First of all the left auricle is the uppermost chamber of the heart and lies almost directly posterior. Just above it is the bifurcation of the trachea; indeed, the left main bronchus normally rests upon it for a short distance. The esophagus passes behind the left auricle and is contiguous with the pericardium overlying it for a distance of several centimeters of its course.

Since the auricle lies posteriorly instead of on the left side of the heart as its appellation designates, it may enlarge as well to the right as to the left, and its proximity to the main bronchi and the esophagus should easily lead to disarrangement of these structures in the course of enlargement.

Enlargement of the auricle to the right was first brought to notice by a report of Owen and Fenton[4] in 1901. In this case there was such massive dullness to the right of the midline that pleural effusion was diagnosed, but thoracentesis in the right axillary line yielded bright red blood, following which cardiac murmurs over the dullness were noted. At post-mortem examination it was proved that the dullness was due to a huge left auricle presenting on the right side.

Other cases of such enormous dilatation of the left auricle have been reported by Emmanuel[5] who describes several older cases from the

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London hospitals, Shaw,[6] Schott,[7] East,[8] Lutembacher[9] and others. Quite recently Bedford[10] has reviewed the subject and added two more cases, and Bramwell and Duguid[11] have established a much more sound pathological explanation of the cause than former observers, namely, fibrosis of the auricular wall.

These enormous dilatations are rare and, hence, not of common interest. A more moderate degree of dilatation, however, commonly occurs and quite frequently is apparent as a part of the right border of the heart in the roentgenogram. From the anatomical studies of Stoerk and the more recent reiteration of Neumann[12] and Assman[13] it is easily understood why the left auricle appears on the right. Neumann interprets the double curve on the right occasionally appearing in mitral stenosis as being made up of the two auricles, the left above, the right below. He also adds that this is seen rarely in cases of aortic insufficiency or arteriosclerosis with left-sided hypertrophy before much enlargement of the right side has taken place. The appearance of the left auricle on the right in such conditions, he believes, is in part due to the rotation of the heart, bringing the left auricle out from behind as in a right oblique view.

In 1922, Bordet[14] in a series of 200 unselected cases of mitral disease noted the appearance of the left auricle on the right side ten times in the outline by x-ray, yet in all of these the auricle was only moderately dilated, and no physical signs were found which might have given a clue to the condition.

In Schott's[7] six cases the auricle was somewhat more prominent, and several presented paravertebral dullness on the right side. This, however, might have been due to small amounts of fluid.

Clinically, then, definite signs of right-sided enlargement of the left auricle are only obtained when the dilatation is relatively enormous, and even then may readily be mistaken for pleural effusion or aneurysm. There may be dullness to the right of the midline extending even as far as the axillary line and murmurs may be heard over this area. Pulsations, visible and palpable, have been reported. It is also of clinical interest that in all of these cases with dilatation of the left auricle to the right in which the clinical findings were stated, auricular fibrillation was also present. This we find occurs in the two cases included in our present report.

The proximity of the esophagus to the auricle was appreciated by Joachim[15] in 1905 and Minkowski[16] in 1906 when they used it as a point from which registration of the presystolic (auricular) impulse was readily obtained. Eichorst[17] states that cardiac hypertrophy may cause compression of the esophagus, but Kovacz and Stoerk[18] were among the first observers to emphasize deviation and compression of the esophagus in enlargement of the left auricle. They injected the esophagus with a soft mass and, on removal of the specimen, demon-

strated three depressions; the uppermost from the bifurcation of the trachea and the left main bronchus, a second from the aorta, and below these a long smooth depression from the left auricle in cases with enlargement of this organ.

They then examined cases of mitral disease by x-ray while the patient swallowed bismuth suspensions or capsules and showed that the esophagus was displaced to the right and backward. The degree of displacement, they thought, was directly proportional to that of cardiac enlargement. In one case a capsule remained just above the compressed area for fifteen minutes which also indicated some obstruction.

Faulkenhausen[19] reported a case of arteriosclerotic heart disease, where compression of the esophagus occurred at two points. The first was at the level of the widened aortic arch; the second at the level of the left auricle which cavity was apparently enlarged, probably due to a functional regurgitation from the hypertrophied left ventricle.

Gabert[20] concludes that the left auricle is almost the sole factor causing compression and displacement of the esophagus, but that its enlargement may very well be part of a general left-sided hypertrophy from causes other than primary mitral disease. The latter condition, however, is responsible most frequently. Gabert also recorded the deviation posteriorly and to the right as former observers had demonstrated.

Rösler and Weiss[21] differ from others in their report, in that the esophagus deviates to the left in some of their cases. Their report deals with seven cases of mitral lesions, four of which were combined with aortic disease. They attributed the displacement to enlargement of the left auricle in all cases and explained the deviation to the left by rotation of the heart which dragged the esophagus, in its passage through the diaphragm, from its normal position just to the right of the midline, over to the left side. This must assume rotation posteriorly from right to left, anteriorly, from left to right, which is in an opposite direction from that found by most observers and contradicts Neumann's observation, that rotation was a factor in aiding the appearance of the left auricle on the right side.

The clinical significance of compression and displacement of the esophagus in patients with enlargement of the left auricle lies in the fact that these patients occasionally have difficulty in swallowing. Two of the patients reported by Rösler and Weiss complained of dysphagia, as did some of the patients in Notkin's[22] report. In the case recorded by Owen and Fenton,[4] previously mentioned, difficulty in swallowing was a prominent symptom and is, of course, frequent in the experience of many.

The development of recognition of compression of the left main bronchus has already been summarized[23] in connection with a detailed clinical report of the first case of this series. Such compression was

first reported by King[24] in 1838. Four cases, three of mitral disease, and one a congenital lesion, were shown at autopsy to have a materially decreased lumen of the left main bronchus resulting from pressure from the enlarged left auricle. Friedreich[25] first clinically diagnosed such a case in 1850 by the lung signs at the left base, the diagnosis being confirmed four years later at necropsy by Virchow. Another case was added by Taylor[26] in 1889 in an autopsy report. There are but few textbooks[27] which mention it, and until Stoerk's[3] admirable anatomical study of the normal relations and those in mitral disease, it received almost no attention. Stoerk combined the measurements of the normal angles at which the bronchi leave the trachea, of Aeby,[28] von Hovorka and Kobler[29] with his own and gave the limits of variation as in Table I (A). The values found in his eight cases of mitral disease are given in Table I (B). It is to be seen that the lower limit in mitral disease corresponds to the upper limit of normal as regards total angle. The case which furnished the minimal total angle (78°) in the series of mitral disease, presented an angle of 61° for the left bronchus. The angle of the left bronchus was, therefore, 12° more than that in any of the normal cases, the small total angle being due to the unusually slight deviation of the right bronchus, namely 17°. The greatest difference, as would be expected, is noted in the angle which the left bronchus makes with the axis of the trachea. This study was carried out on autopsy material.

Two years later, Kahler[30] by bronchoscopic examination of patients with mitral disease from Kovacz' clinic, was the first to demonstrate displacement of the left main bronchus in living subjects and showed that some compression was present in all but one of the thirteen cases, the narrowing of the lumen occasionally being extreme. In only one of these cases were there signs of pathological nature noted at the left lung base.

Quite recently Gabert[31] in x-ray studies of the heart was able to visualize the main bronchi in anteroposterior and lateral views. The comparison of his cases of mitral disease with the normal leaves no doubt that spreading of the angle of departure of the main bronchi from the trachea occurs with an enlarged left auricle. That the elevation pertains especially to the left main bronchus was in accord with former observers.

It appears that it is only in the small minority of cases, those with extreme compression of the left bronchus, that clinical signs become manifest. Usually the phenomenon has been found at autopsy or by special examination without a previous clinical diagnosis. The physical signs appear only when secondary lung changes take place, such as atelectasis, or chronic infection and bronchiectasis which require rather marked obstruction for their production. Then we find persistent moisture, stridulous respiration, and even dullness with breath sounds

which may vary from a diminished vesicular murmur to loud tubular breathing. They may be coupled with long continued fever, cough, and expectoration of sputum. Such signs have occurred in the past, but only once, and that three-quarters of a century ago, has a diagnosis been made on that basis. This was made by Friedreich[25] in 1850.

X-RAY STUDY

The Outline of the Auricle.—

The examination is made both fluoroscopically and roentgenologically, the patient being examined in the anteroposterior position, in both oblique positions and in the lateral position. In the right oblique position the right breast is against the film or screen; in the left

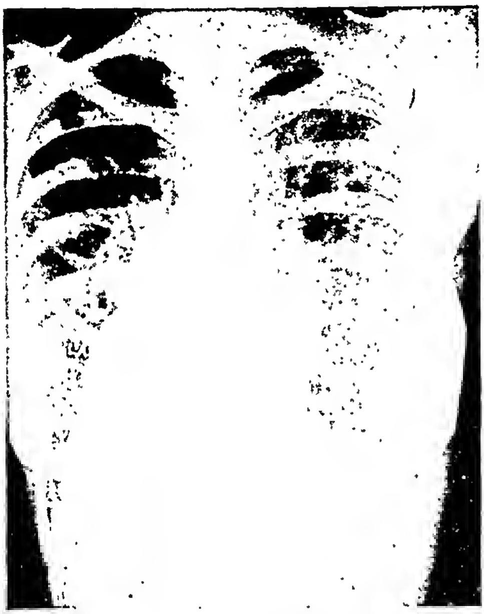

Fig. 1.

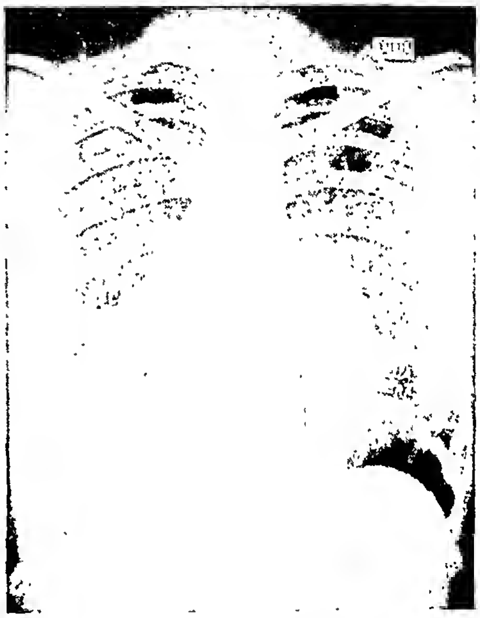

Fig. 2.

Fig. 1.—Case 3 showing the mitral shape of heart. L.V., left ventricle; L.A., left auricle; P.C., pulmonary curve.

Fig. 2.—Case 2 showing how the enlarged left auricle may project beyond the normal right border of the heart. Both auricles identified at fluoroscopy.

oblique, the left breast. In oblique and lateral rays of a normal chest there is no marked protrusion of any part of the back of the heart into the clear space of the posterior mediastinum.

The shape of the heart known roentgenologically as the mitral type is well recognized (Fig. 1). Vaquez and Bordet[32] deal very fully with this aspect of the subject in regard to the heart outline of this type in anteroposterior as well as in oblique views. The characteristic features from the front are an increase in the horizontal diameter, a widening above the ventricles, and the presence of an extra curve (L.A.) between the pulmonary cone shadow (P.C.) and the left ventricle (L.V.). In the lateral and in the right oblique positions the posterior surface

of the dilated auricle is smoothly spherical and shows as a definite, backward bulge about two to three inches above the diaphragm. The differential diagnosis of these films is, however, not easy.

That the left auricle, if enlarged, shows clearly in the right oblique position and may show even in the anteroposterior position as the upper portion of a double shadow on the right side (Fig. 2) is not so well recognized. The identity of this double shadow can be verified at fluoroscopy; a slight rotation to the right bringing the upper shadow into greater prominence, hence showing it to be posterior. A study of the pulsation may also help. In one of our cases, which was fibrillating, we found on fluoroscopic examination that these two curves pulsated asynchronously. During ventricular systole the left auricle

Fig. 3.

Fig. 4.

Fig. 3.—Case 1. Front view of chest while patient swallows barium emulsion, showing how the enlarged auricle displaces the esophagus to the right.

Fig. 4.—Case 3. Lateral view of chest while patient swallows barium emulsion, showing backward displacement and compression of the esophagus.

was ballooned out under pressure from the left ventricle through the incompetent mitral valve, while the right auricle, protected from pressure by the competent tricuspid valve, did not balloon out but rather seemed to contract.

Examination of the Esophagus.—

Examination of the esophagus in cases of mitral disease is not new but merits more common use in roentgenological examination. The patient is examined during the act of swallowing a thin barium suspension. Fluoroscopy is sufficient unless permanent records are desired. The normal esophagus passes directly down the mediastinum with a slight inclination to the right at about the middle of the thorax.

In the lateral views the indentations of the backs of the tracheal bifurcation, the aortic arch, and the left auricle on the anterior wall of the esophagus can be observed but are never prominent. An enlarged auricle presses the esophagus backward and, usually, to the right (Figs. 3 and 4), and on fluoroscopy the pulsation of the auricle, transmitted to the fluid barium in the esophagus, is strikingly shown. Since the displacement is to the right and backward, it should be seen at its maximum in the right oblique position (Fig. 5) and at the minimum in the left oblique position. In the latter position the esophagus should appear straight, as it is examined in the plane of the curve. This we found to be the case.

We have examined by this method a number of cases of heart disease other than mitral—including two enormous hearts, one in a case of hypertension and one in a case of congenital heart disease. In all of these the esophagus followed its normal course or was deviated to an extent which was relatively slight compared to the degree of general enlargement of the heart. In some cases of early mitral disease, too, the esophagus was normal in position, but in these, evidence of auricular enlargement was also lacking. One of us in examining a few cases of known mitral disease in young children found this same deviation of the esophagus in well-established cases. We have not observed any deviation to the left as was noted by Rösler and Weiss.[21]

Examination of the Trachea and Main Bronchi.—

The fact that enlargement of the left auricle may cause displacement and distortion of the bronchi has long since been shown on the autopsy table. It has only recently been demonstrated by x-ray. This was done by Gabert[31] in 1924 in anteroposterior views in which the main bronchi showed dimly but plainly enough to estimate the angle between them. By the use of the left anterior oblique position in addition to the anteroposterior view we find that we can visualize the bronchi more clearly and more frequently. By raying more densely and by the use of lipiodal in stout subjects, we can nearly always outline the course of the trachea and main bronchi. It is essential that films be made, for visualization of the bronchi under the fluoroscope is unusual unless lipiodol is used.

In anteroposterior films of the chest, the normal position of the bifurcation of the bronchus lies just to the right of the lower edge of the rounded shadow of the aortic arch in the left upper mediastinum. The angle between the right and left bronchi varies from 40 degrees to 70 degrees (apparently depending to some extent upon the build of the patient), as measured in a series of 6 foot anteroposterior films of normal chests after lipiodol injection. The average angle in twenty normal cases was 58 degrees with a maximum of 70 degrees and a minimum of 38 degrees. Allowing for the fact that the apparent angle in the film may be rather less than the real angle, these results

agree quite well with those of Stoerk.[3] In the left oblique position, which we found most useful in demonstrating bronchial abnormality, the angle is some five to ten degrees less than that of the corresponding anteroposterior films. In this same view, normal individuals usually show a certain amount of space between the shadows of the back of

TABLE 1

VALUES OF THE TRACHEOBRONCHIAL ANGLES (FROM STOERK)

(A) Normal			
	RIGHT	LEFT	TOTAL
Average	24.38°	44.89°	69.27°
Extremes	19° to 35°	32° to 49°	58° to 78°
(B) In Mitral Disease			
	RIGHT	LEFT	TOTAL
Average	34.8°	60.3°	95.1°
Extremes	17° to 52°	51° to 73°	78° to 117°

the heart and left bronchus. Fig. 12 (A and B) shows tracings of the bronchi made from films taken after injection of lipiodol and illustrates the diminution of the bronchial angle in the change from the anteroposterior to the left oblique position. In stout subjects, especially, for anteroposterior views it may be necessary to inject a small amount of lipiodol to visualize the bronchi. In the left oblique view which was found more convenient and reliable for outlining the bronchi than any other, the procedure is seldom needed but is so simple and well established that its use seems justified in any case of cardiac enlargement in which there is doubt concerning the correctness of the diagnosis.

We have studied in considerable detail five cases of typical mitral disease and many of less certain clinical diagnosis. Observations were made also on several other types of heart lesions. That one may judge their value, summaries of these five clear-cut cases of mitral disease are included, as they have not yet come to autopsy. The illustrations are taken from these cases entirely except Figs. 10, 11, and 12 (A, B, C, D). The illustrations and the measurements of normal angles were made from films of individuals suspected of bronchiectasis in whom lipiodol was used and who showed no evidence of cardiovascular disease, or of pulmonary disease, sufficient in any way to admit of the possibility of bronchial distortion.

CASE SUMMARIES

CASE 1.—A white man, 47 years old, with symptoms of cardiac insufficiency for ten years and twice decompensated entered the medical service, after an acute febrile illness of five weeks, having developed a stabbing pain in the left chest the night before admission. Dyspnea and cough with a production of large amounts of purulent sputum were the chief complaints. He was dehydrated and dyspneic with a large heart, auricular fibrillation, a systolic blow and a low diastolic mur-

mur. The first sound at the apex was short and sharp, and the second pulmonic sound was much increased. The lungs were filled with moist râles, most numerous over the left base where there was dullness and a friction rub. The electrocardiogram showed auricular fibrillation and right ventricular predominance. Routine x-ray examination revealed an extra convexity of, and an increase in width of the left upper border. Further examination showed the esophagus displaced posteriorly to the right (Fig. 5) and a protrusion of the upper portion of the cardiac shadow posteriorly.

Improvement occurred slowly but after five weeks with the patient up and about on the ward, the râles and dullness at the left base posteriorly, persisted. The breath sounds varied, sometimes suppressed, and sometimes tubular in quality. The production of sputum continued at the rate of from two to four hundred c.c. per diem. Bronchiectasis was suspected, and an x-ray examination following lipiodol injection was done. There was no bronchiectasis, but the angle be-

Fig. 5.

Fig. 6.

Fig. 5.—Case 1.—Right oblique view of chest while patient swallows barium, showing the esophageal displacement is most apparent in the right oblique position. A small diverticulum is present.

Fig. 6.—Case 1. Front view of chest after lipiodol injection of the bronchi showing distortion and compression of the left bronchus by the enlarged left auricle.

tween the bronchi was increased to approximately 90 degrees, and the left bronchus was turned upward and compressed at a point about 1½ cm. from the bifurcation of the trachea. The course could be made out in the anteroposterior film (Fig. 6) but was better seen in the left oblique position. In the latter, it could be followed even without the use of lipiodol (Fig. 7).

At the present time the physical signs at the left base persist as well as cough and production of moderate amounts of sputum, yet the patient is at home and now driving a taxicab nine months after his admission.

Case 2.—A white woman, 24 years old, was admitted March 7, 1928, complaining of dyspnea and palpitation, first noted five years previously during the first pregnancy, recurring more severely during the second pregnancy one year later. Since then she has been free from symptoms, save on considerable exertion, until

two weeks before admission when a rapid increase in dypsnea occurred with the onset of almost continuous palpitation. On examination she was dyspneic, yet without any signs of congestive failure, the heart was quite large, 4 cm. to the left in the third interspace, 11 in the fifth, and just to the right of the sternum in the fourth. The apical rate was 140, and auricular fibrillation was proved by the electrocardiogram. Systolic and diastolic murmurs were definite, both best heard in the fourth left interspace. The x-ray and fluorscopic examinations revealed a heart greatly enlarged to the left and right, a biconvex right border, the two convexities of which pulsated asynchronously. There was a large backward bulge of the upper posterior border in the lateral view, which pulsated actively and on which the barium in the esophagus, which was displaced posteriorly and to the right, danced with the transmitted pulsation. The left oblique view showed a widening of the bronchial angle to 80 degrees and some compression and upward displacement of the left bronchus. A diagnosis of rheumatic endocarditis

Fig. 7.

Fig. 8.

Fig. 7.—Case 1. Same as Fig. 6 in the left oblique position showing the compression and elevation of the bronchus very clearly.

Fig. 8.—Case 3. Left oblique view of the chest showing how distortion of the left bronchus can be seen in this position without previous lipiodol injection; contrast with Fig. 9.

with double mitral disease, insufficiency of the valve being more prominent, was made. The rate was easily controlled with digitalis, rapid improvement followed, and the patient is quite well doing housework at home.

Case 3.—A white girl, 26 years old, entered the hospital on Feb. 28, 1928, with the complaint of heart trouble. The history suggested acute rheumatic fever at eleven years of age, and she had been sent to a sanatorium three years prior to admission, for pulmonary tuberculosis. Cardiac symptoms had been present only one year, beginning with dyspnea, then attacks of nocturnal orthopnea, and for a few months edema of her ankles. The patient had been in bed for some months and on admission at rest showed no signs of cardiac insufficiency except slight cyanosis of the lips, not visible in the finger tips. The heart was moderately enlarged, regular, slow; the apical impulse was forceful, and there was a systolic shock. A loud crescendo presystolic murmur, heard best in the third and fourth

left interspaces inside the midclavicular line, and a soft systolic blow at the apex, were present, together with a snapping first sound at the mitral area, and made the diagnosis of rheumatic endocarditis with mitral stenosis quite definite. There was no evidence of pulmonary tuberculosis on physical examination. The electrocardiogram showed a notched P-wave in Leads I and II and a right ventricular predominance. X-ray examination revealed a moderately enlarged heart with a mitral configuration (Fig. 1). The lungs were clear. The esophagus was displaced backward (Fig. 4) and to the right. The left main bronchus was elevated (Fig. 8), making a total bronchial angle of 70 degrees, and bent upward about 3 cm. from the bifurcation. These findings served to confirm the clinical diagnosis.

The patient improved and six months later is still returning to the dispensary in about the same condition. Her physical activity is very limited, the cyanosis remains unchanged, but as yet no signs of congestive heart failure have made their appearance.

Fig. 9.

Fig. 10.

Fig. 9.—Left oblique view of the chest in a normal individual after lipiodol injection showing the normal bronchial angle in this position and the normal course of the left bronchus in contrast to Figs. 7 and 8.

Fig. 10.—Front view of the chest showing position of bronchi in a case with enlarged heart not due to mitral disease (case of patent ductus arteriosus) showing widening of bronchial angle but no distortion of the bronchus.

Case 4.—A salesman, 43 years old, was seen in our out-patient department on Dec. 23, 1927, and subsequently admitted to the hospital, for study rather than therapy. His complaint was "shortness of breath and substernal pain." A definite history of acute rheumatic fever at the age of 31 and again at 36 years was obtained. Symptoms of dyspnea, palpitation, choking and dull precordial pain, usually only on effort, had been present for four years without much increase until one month before admission when a constant cough developed. On examination the patient presented an unusually slow pulse rate, 48 to 56, irregular, and unaffected by atropine. The heart was much enlarged, 13 cm. to left in the fifth interspace, and a systolic murmur and a long diastolic murmur were heard. The first sound was short and snappy at the apex. The electrocardiographic record was that of auricular fibrillation with a very slow ventricular rate occasionally with thirty or forty second intervals. The configuration of the heart in the x-ray film

was typical of the enlarged left auricle, the esophagus was displaced posteriorly and to the right. There was some widening of the bronchial angle to the upper limit of normal, namely 70 degrees. The upturning of the left bronchus 2 cm. from the bifurcation was well marked in the left oblique view. A diagnosis of rheumatic endocarditis with mitral stenosis was made.

The patient continues to return to the cardiac clinic, his clinical condition unchanged save that in spite of the low ventricular rate, the dyspnea and precordial pain seem slightly alleviated by digitalization.

Case 5.—A salesman, 32 years old, came to our clinic first on Feb. 9, 1928. He had an indefinite history of acute rheumatism at the age of 14 years, and a typical attack of acute rheumatic fever at 26 years. Tonsillectomy was performed at 12 years of age because of frequent tonsillitis. Since the second attack of rheumatic fever six years before, dyspnea and dull precordial pain after exertion have been constantly present. Two years before examination he had several very small

Fig. 11.—Left oblique view of the chest in a case of enlargement of the heart due to hypertension showing widening of the bronchial angle but no distortion.

hemoptyses and recently sudden attacks of dyspnea. The general examination was altogether negative. The heart was slightly enlarged to percussion, especially the upper left border, 5 cm. to left in third interspace, and a systolic murmur and crescendo presystolic murmur with a palpable thrill were present. Predominance of the right ventricle and notched auricular waves (Leads I and II) were noted in the electrocardiogram. The anteroposterior x-ray of the chest showed a well-marked curve between the pulmonary cone and left ventricular shadows. The lateral and left oblique views showed a posterior bulge of the cardiac shadow near the base, leaving the lower portion of the retrocardiac space clear. In the left oblique view the main bronchi were visualized and the angle between them measured 70 degrees while the left main bronchus showed a well-marked upward deflection 3 cm. from its origin in the trachea. The diagnosis of rheumatic endocarditis with mitral stenosis was made. His condition at present is unchanged. He is still carrying on his business and was advised to take a few hours additional rest.

Wassermanns on all these patients were negative. Unmentioned routine laboratory tests were either of little importanee in the present eonneetion or negative.

COMMENT

With regard to the outline of the enlarged left auriele, the appearanee of the eurve L.A (Fig. 1) is now generally reeognized as pertaining to this organ, but we should like to emphasize the faet that the

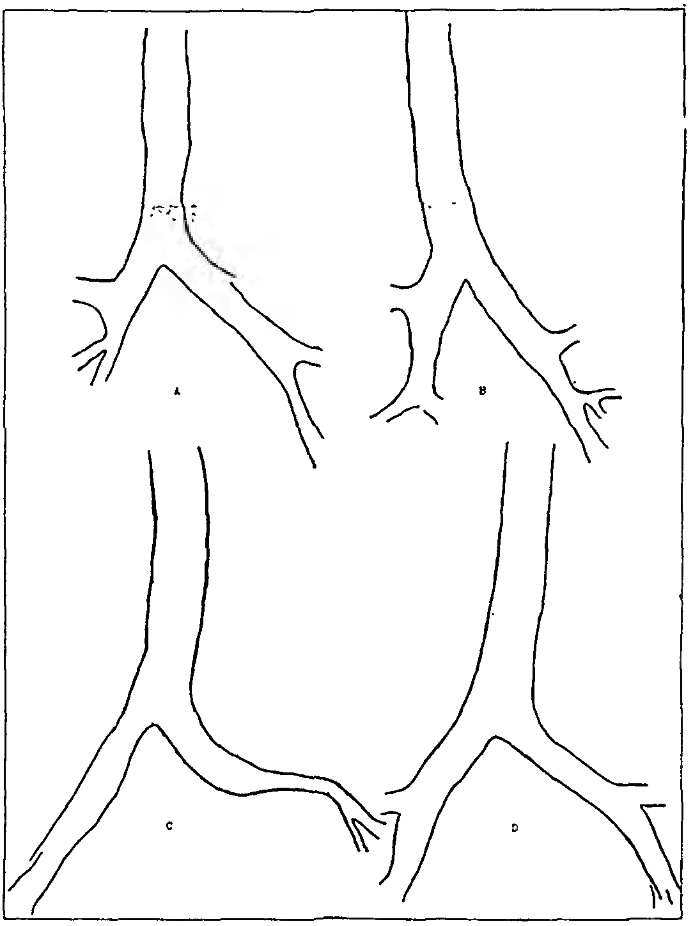

Fig. 12.—Traeing of traehea and bronehi made from films taken after lipiodol injeetion. (A) Normal ease with average bronehial angle as seen in front view. (B) Same ease, as seen in left oblique position. (C) Typieal instanee of elevation and eompression resulting from enlargement of the auriele. (D) Widening of the bronehial angle without distortion assoeiated with enlarged heart not due to mitral disease.

left auriele may appear as part of the upper right border of the heart in x-ray films long before it is detectable in physieal examination. (Cases 1 and 2.) Fluoroseopy is here essential for two reasons. First, gradual rotation of the patient to the left aseertains that this upper eonvexity of the right border is identical with the posterior bulge of the heart. This in turn is generally agreed to be left auriele. Seeond, the oeeasional helpful finding of asynchronous pulsations of the two eonvexities, as noted in Case 2, may be present.

The deviation of the esophagus in mitral disease is well known but is not sufficiently used as a routine test. In passing, it may be noted that it has always been to the right and backward in our experience, as most observers have recorded. It does not usually occur to any noteworthy extent, even in cases of enormous cardiac enlargement unless the left auricle is involved in the enlargement.

Distortion of the left bronchus as a useful indication of left auricular enlargement is practically unknown. The result of the x-ray examination after lipiodol injection in Case 1 was rather a surprise, although the possibility of compression of the left bronchus as a cause of the lung findings in the left base had been suggested. The markedly widened bronchial angle of 90 degrees, the compression and especially the upturning of the left main bronchus (Figs. 6 and 7) precipitated this study. At that time we were unaware of Gabert's work. Then, when the left oblique views were found to show the bronchi still more clearly, and when by raying more densely it was possible to demonstrate the outline of the bronchi with a certain degree of regularity, the possibilities of a useful diagnostic method appeared.

In no case of known mitral disease was the bronchial angle less than 70 degrees, which we have already seen to be the upper limit of normal; while in the most marked cases it was over 90 degrees. The same 5 to 10 degrees less in the oblique views was true here as in the normal cases. The reported angles ranged from 90 to 70 degrees.

The notable feature about this distortion was not so much the widening of the bronchial angle as the manner in which the bronchus curved gradually upward, instead of the normal straight or downward curvatures. (Fig. 8.) The obvious elevation and distortion of the bronchus is easily observed as contrasted with the normal (Fig. 9). The same contrast is noticeable in the diagram in Fig. 12 (C) which illustrates the type of displacement and the manner in which the bronchus may be compressed.

We have examined also, several cases of cardiac enlargement due to causes other than mitral disease and have found that a moderate widening of the bronchial angle may occur, but to a much less extent for a heart with the same degree of enlargement. Neither have we ever observed in cases of heart disease other than those associated with auricular enlargement, the characteristic upturning and compression of the bronchus (Figs. 11 and 12 [D]).

An excellent illustration of this difference is to be found in Fig. 10 (compare with Fig. 6). This was a case of enormous cardiac enlargement in a Filipino man of 25 years, who had had symptoms of heart disease for three or four years, and in whom a definite diagnosis could not be made between a congenital heart lesion and rheumatic valvular disease. For two reasons it seemed certain that the left auricle did not participate to any great extent in the enlargement. First, there was no pro-

trusion of the posterior portion of the heart into the retrocardiac space. Second, we were able to demonstrate by lipiodol injection that the bronchi pursued a normal course save for a possible slight widening of the bronchial angle to 75 degrees, only 5 degrees above the upper limit of our normal series. This was the only change in spite of the fact that the enormous heart shadow bulged well to the left of the left bronchus (Fig. 10). Were the upper left shadow left auricle, the bronchus would be bent upward, compressed and would tend to ride the shadow.

At autopsy some pulmonary sclerosis and a very large patency of the foramen ovale (3 cm. in diameter) was all that could be found to explain the enlargement. The heart weighed 900 grams and the enlargement was mainly right sided, the right auricle, right ventricle and pulmonary cone and artery being enormous. The left auricle was little, if any, enlarged. This readily explains why the left bronchus was relatively undisturbed, since the pulmonary cone and artery are free to enlarge to the left anterior to the left bronchus, not bound under it as is the left auricle.

The only other conditions in which we have observed a distortion of the left bronchus similar to that found in enlargement of the left auricle are tuberculosis and tumor of the lungs. Extreme fibrosis or contraction of the left upper lobe may result in widening of the angle of deviation of the left bronchus, and even in the characteristic upturning noted in enlargement of the left auricle; but the obviousness of a pulmonary lesion sufficiently large to give this result precludes any confusion.

SUMMARY

The left auricle has a peculiar anatomical position, in that it is the posterior and superior chamber of the heart, thereby being in closest relation to the esophagus and to the bifurcation of the trachea. By virtue of this position the left auricle may enlarge to the right as well as to the left and during the course of its enlargement may exert pressure on the esophagus and main bronchi. There are many reports in the literature illustrating these effects, the least known of which is the last. Compression and displacement of the bronchi but rarely give rise to lung changes, yet may be frequently found by x-ray, and together with displacement of the esophagus are usually attributable to the left auricular enlargement.

Roentgenological methods demonstrating the occurrence of these three phenomena are described which make more accurate the diagnosis of enlargement of the left auricle.

1. Observation of right border of the heart for double curve in anteroposterior films and fluoroscopy to verify that the upper curve is identical with the posterior superior curve of the heart, and to note

asynchronous pulsations of the two curves. This last makes the diagnosis of left auricular enlargement quite definite.

2. Observation of displacement of the esophagus. The esophagus is displaced posteriorly and to the right by left auricular enlargement.

3. Demonstration of bronchial displacement, particularly as noted in the films made in the left oblique position in obese patients, after an injection of lipiodol. Bronchial compression and displacement in left auricular enlargement occur frequently and can be demonstrated by x-ray study, as by left oblique views, also in anteroposterior views following lipiodol injection.

Note.—Since sending this article to the publishers the very excellent description of the position and relation of the left auricle has come to my notice: David Steel, "The Roentgenological Findings in Mitral Stenosis and Insufficiency," Amer. Jour. Roent. 21: [illegible], March, 1929.

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TRANSITORY VENTRICULAR FIBRILLATION AS A CAUSE OF SYNCOPE AND ITS PREVENTION BY QUINIDINE SULPHATE*

With Case Report and Discussion of Diagnostic Criteria for Ventricular Fibrillation

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THE diagnosis of ventricular fibrillation cannot be proposed for electrocardiograms of patients with the assurance usual in classifying records of arrhythmias. The experimental evidence on which the interpretation of the curves must be based has not been so thorough or convincing that one may state whether any questionable record should be classified as ventricular tachycardia, flutter or fibrillation. With these facts in mind I wish to present a patient with syncopal attacks as the presenting complaint, in whom during such an attack, induced by injecting epinephrine, ventricular arrhythmia of bizarre type was recorded.

CASE REPORT

Mr. E. S., married and father of several normal children, had been subject to dyspnea and fatigue on exertion "all his life." Between the ages of 28 and 33 years he had numerous attacks of arthritis of knees and ankles, with little or no fever.

He was 36 years old when he had his first syncopal attack, which occurred while he was at rest. Three weeks later he had a similar attack, and these attacks occurred at intervals of about one month from April, 1926, until April, 1927. They then became more frequent and variable in severity up to October 15, 1927. Between October 15 and 25 they occurred one or more times daily. He had always considered himself a nervous man, and this irritability was increased at this time. The noise made by his children often was the precipitating factor for the attacks.

He described his attacks as follows: A sudden sensation of heaviness in the chest seized him, and seemed to well up toward his head. The skin felt as though warm water were rising over it. When the sensation reached the chin level, he became weak and had to hold on to something to keep from falling. When it reached the level of his nose, he lost all muscular control, became blind and fell to the floor. He thought he had only lost consciousness once, and then for two minutes. Usually the attacks stopped before he became blind, and after the attacks passed off he was weak and tremulous for from twenty to thirty minutes. During the attacks his physician noted that pulse and heart sounds were absent.

On October 26, while in the office of Dr. R. B. McKenzie, he had a mild attack, the termination of which was recorded electrocardiographically (Fig. 1). He then entered the hospital and during five days of bed rest had no attacks.

He was a well-developed man, somewhat over-alert but not sick. There was marked dental caries with pyorrhea. The heart and lungs were quite normal, blood pressure

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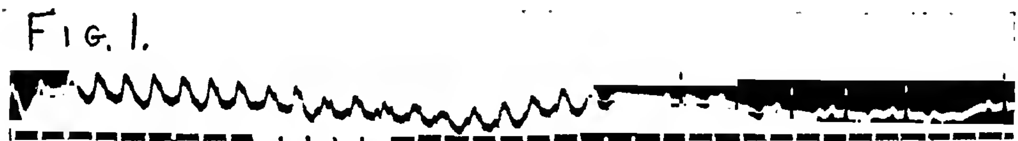
was 140 mm. systolic, 85 mm. diastolic. The blood, urine, Wassermann and teleroentgenogram of the heart were all normal. The electrocardiogram was normal except for rare ventricular extrasystoles, all arising in the same region.

The patient was given epinephrine 0.2 c.c. of 1/1000 solution intravenously. Marked nervousness, tremor and sinus tachycardia occurred; no extrasystoles were produced. Within ten minutes the effect had almost entirely subsided. Fifteen minutes after the first injection a second dose of 0.3 c.c. was given. Before the record (Fig. 2) was started or the needle was out of the vein, the attack came on, and this was quite typical of the attacks observed by his home physician several times in the previous two weeks, during which the patient was pulseless, no heart sounds were audible and weakness and blindness came on within half a minute. The whole attack lasted about one minute, but he was very weak for half an hour.

He was put on constant medication with quinidine sulphate 0.3 gm. three times a day and in the year following this had but one attack of syncope. This was



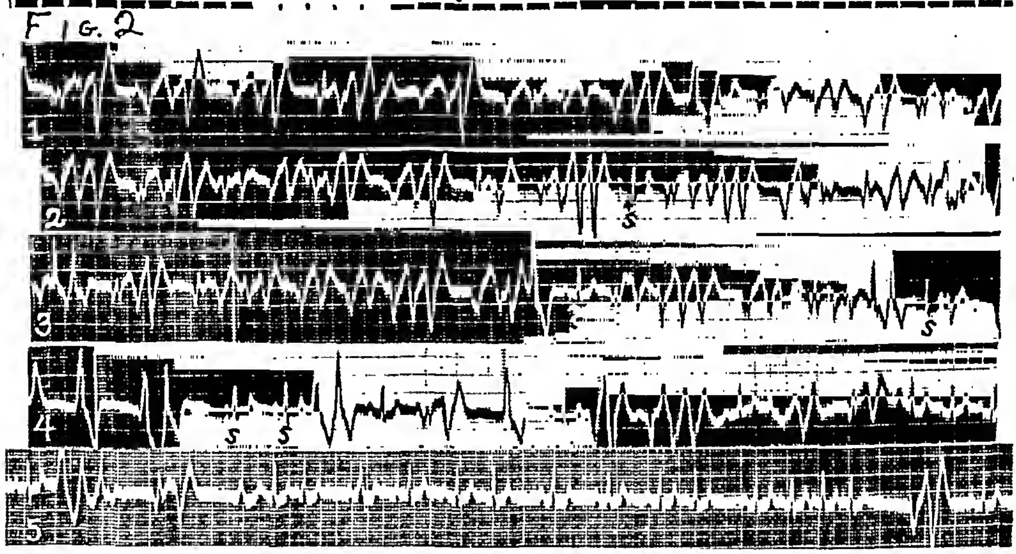


Fig. 1.—Termination of spontaneous attack of ventricular arrhythmia, rate 285 per minute. Time in 1/5 seconds.

Fig. 2.—Consecutive tracings during an attack induced by epinephrine. Two seconds of sinus rhythm omitted between Nos. 4 and 5. Note sinus beats (marked with *S*) interpolated without postundulatory pause in Nos. 2 and 3.

during the removal of his carious teeth under local anesthesia. He found that when he discontinued quinidine for a few days he was troubled by fleeting sensations of precordial heaviness, and this difficulty persisted even after his gums had been healed over for six months. His tendency to fatigue easily and to become short of breath on exertion was unchanged.

Summary.—A middle-aged man, who had always had symptoms suggestive of effort syndrome, had syncopal attacks with increasing frequency for eighteen months. After quinidine rationing the attacks no longer occurred. Electrocardiograms were obtained during one mild spontaneous and one severe attack induced by giving epinephrine.

DESCRIPTION OF ELECTROCARDIOGRAMS

The tracing (Fig. 1) obtained during a brief spontaneous attack shows a ventricular tachycardia (rate 280), with moderate variation in shape and duration of electrcial complexes. There is no iso-electric period. The normal rhythm begins after a short pause; it is at first rapid but soon returns to a rate of 58 per minute.

The tracing (Fig. 2) obtained during the attack induced with epinephrine is of an entirely different sort. The ventricular rate varies between 190 and 200 per minute, although toward the end of the attack much slower rates of deflection can be noted for 2 to 4 complexes. There is no dominant form of electrical complex but the widest variation in shape with a tendency to have a few more or less similar waves followed by groups wholly different. About thirty seconds after the beginning of the attack a single sinus beat of normal shape, and not preceded by a pause, is interpolated in the tachycardia. Similar beats occur more frequently, then in twos and threes, and finally the attack terminates in a run of rapid sinus beats with occasional brief runs of abnormal ventricular complexes.

DISCUSSION

The cardiac activity represented by the oscillations recorded in Fig. 2 is obviously of quite a different order from the usual ventricular tachycardia, and it may be doubted that this attack induced with epinephrine is the same as the patient's spontaneous attacks. Subjectively the attack was quite like his severe seizures, and we know that in other cases where similar doses of the drug have been given to patients with a tendency to ventricular arrhythmia the effect was to produce attacks which were quite similar to the spontaneous ones[1] or to cause merely a sinus tachycardia.[2] In this patient a dose only one-third smaller had evoked no ectopic rhythm.

To classify these tracings it is necessary to review those ventricular arrythmias which lie beyond simple tachycardia. In the German literature[3] the same scheme is used as with the auricular arrhythmias, and they designate as flutter those with continuous dentate oscillations of fairly regular form, and as fibrillation those with irregular and rounded oscillations. English and French authors avoid the term "ventricular flutter" and substitute "pseudofibrillation," "phase ondulatoire" or "those preliminary disturbances which precede" fibrillation.[4] These observers attach prognostic rather than physiological significance to these distinctions, for as MacWilliam[5] states of the conditions in the exposed heart of experimental animals, "from the evidence afforded by inspection, palpation, tracings of the oscillations, fall of blood pressure, etc., the two conditions (fibrillation and pseudofibrillation) may be impossible of distinction, but they differ strikingly as regards persistence; pseudofibrillation ceases immediately or at vary-

ing short periods after the cessation of the stimulation, while true fibrillation under ordinary circumstances goes on as a rule to the death of the heart.'' This distinction between fibrillation and the stage which precedes it, based wholly on prognosis, is of no value in human physiology, for the tendency of fibrillation even when fully developed in man is toward early spontaneous arrest of the arrhythmia. No one would accept a division of auricular fibrillation into pseudo and true on a basis of persistence, although here the difference in duration of paroxysmal and permanent attacks is a question of years. It is obvious that such a distinction is even more absurd for ventricular fibrillation where persistence for eight or ten minutes means death. With regard to the distinction between flutter and fibrillation, it is well to recall that in auricular flutter it is possible to demonstrate A-V conduction, usually with partial block, as well as motion of the auricles and of blood in the great veins due to the fact that the auricular muscle still contracts as a unit. Similar motion of ventricular muscle has never been demonstrated in the so-called ventricular flutter in man. Lewis[4] has shown that in the early stage of ventricular fibrillation in the dog the oscillations are quite similar in regularity and shape to the dentate oscillations of auricular flutter; yet at this time the carotid pressure scarcely fluctuates from zero, and the ventricular myocardiogram is a straight line. It seems certain that we will have to content ourselves with the diagnosis of tachycardia for those cases where persistent heart sounds or other pulsatile activity of ventricles is present, and fibrillation for those where gross mechanical arrest is present with persistent electrical oscillations. The more rapid and irregular these oscillations, the more certain can we be of advanced disturbance in the conduction of the circus movement, but slower and more regular oscillations are compatible with a dilated and fibrillating ventricle as may easily be observed with the exposed dog heart.

With these facts in mind it seems quite proper to suggest that both attacks recorded in this patient were due to ventricular fibrillation, the spontaneous one having a more rapid and regular oscillation than the induced attack. The conditions under which the latter occurred, the slower rate and great number of brief pauses suggest that the condition resulted from the depressant action of epinephrine, rather than from its sympathecticomimetic action.

This brings us to a consideration of the factors which produce or initiate ventricular fibrillation.[6] Experimentally fibrillation can be produced by faradization, and even in some species by a properly timed single shock to the ventricle or by massage or heating, by ligation or injection of emboli into the coronaries, or by alterations in vagal and sympathetic tone. A wide variety of drugs produces this arrhythmia: potassium, barium, pilocarpine, quinidine, digitalis, nicotine, cocaine, chloroform and epinephrine. The latter is unique in that small doses

may cause and large ones arrest ventricular fibrillation. Clinically the following facts seem well established: electric shocks, chloroform anesthesia and disease of coronary arteries may cause ventricular fibrillation and death. The great majority of clinically recorded cases of ventricular fibrillation occurred in patients with permanent A-V block shortly before death from myocardial disease or at the time of death in patients with other diseases. It has been assumed that sudden death occurring after emotional shocks, or in patients with angina pectoris, aortic insufficiency and the like are due to ventricular fibrillation, and deaths from digitalis and from quinidine are attributed to a similar mechanism. In patients with advanced myocardial disease the tendency to ventricular arrhythmia, especially under digitalis, is marked and may terminate in fibrillation.

We noted previously that of the score of cases of ventricular fibrillation recorded electrocardiographically, only one in a patient dying of heart disease, and two in cases in which the dying heart was recorded in patients with infectious disease were truly terminal, all the rest were transitory and this, in spite of the unfavorable conditions—complete heart-block, quinidine poisoning or moribund febrile state—which led to the occurrence of the arrhythmia. The most rapid ventricular fibrillation ever recorded in man terminated abruptly and the patient recovered,[7] while in thirty-seven moribund patients studied by various groups, only five showed transient fibrillation and two terminal fibrillation.[8, 9, 10, 11] I think that we must conclude from this that ventricular fibrillation is not easily established or maintained in man.

Nothing has been reported concerning treatment of attacks or prophylaxis in man. If we may judge from animal experiment, the intracardiac administration of full doses of epinephrine, or of potassium chloride, chloral hydrate or camphor would be worthy of trial in the attacks, and quinidine or digitalis as prophylaxis. We used quinidine in this case because of Scott's report[1] of its effectiveness in ventricular tachycardia, and the result seems to have been excellent.

SUMMARY

The significance and diagnosis of ventricular fibrillation is discussed with reference to a patient without evidence of organic heart disease, who had for eighteen months attacks of syncope due to transitory ventricular fibrillation. Quinidine sulphate rationing prevented these attacks.

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ELECTROCARDIOGRAPHIC CHANGES IN DIPHTHERIA

II. Intraventricular Block*

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One of the most striking clinical features in some cases of diphtheria is the extreme toxicity of the patient with a condition of the circulatory system bordering on collapse. Low blood pressure and feeble peripheral pulses, poor heart sounds and gallop rhythm are indications of cardiac dilatation, which is demonstrable clinically and has been observed roentgenologically. Such signs may be associated with slow or rapid heart rates and with irregular rhythms suggesting heart-block or independent ventricular tachycardias, which give serious prognosis. Electrocardiographic studies often reveal only a normal cardiac mechanism with intraventricular block varying from merely delayed QRS interval to typical bundle-branch block.

It is the purpose of this paper to call further attention to these phenomena and to consider the progress of these abnormalities from rather mild effects to more severe ones and to death in some cases, or to complete clinical and electrocardiographic recovery in others. Six cases were studied. Many other instances of delayed intraventricular conduction were observed, but they were accompanied by complete heart-block and have been considered in a previous article.[1] This paper suggests that the intraventricular block is frequently the result of a functional depression of the conduction system, rather than an anatomical change.

A brief summary of the cases and a description of the records follow. Measurements were made by projecting electrocardiographic films on a screen so that time intervals of 0.04 second equalled 0.5 inch. Readings were taken with a ruler.

CASE REPORTS

Case 1.—A negro boy, 5 years old, received 40,000 units of antitoxin on admission to the hospital. As no clinical history was ever obtained, the previous duration of illness remained unknown. The patient was very sick with low blood pressure and a pulse rate of 120 for six days, followed by marked improvement. On the twenty-seventh day in the hospital, nystagmus and petechiae of the skin appeared, and lumbar puncture showed 152 mononuclear cells and globulin. A diagnosis of tuberculous meningitis was made. Death occurred the next day after clonic convulsions.

An electrocardiogram on the ninth day in the hospital shows normal mechanism with regular rate of 80. The P-R interval is about 0.18 second. Ventricular com-

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plexes show splintering, they are diphasic in Leads I and II, and inverted in Lead III. The QRS interval varies from 0.13 to 0.14 second in Lead I. The T-wave is upright in all leads (Fig. 1). A record taken on the following day is similar, but the excursion is greater in Lead I (Fig. 2). The next record, taken on the eleventh day, is similar to the first two described except that the splintering of

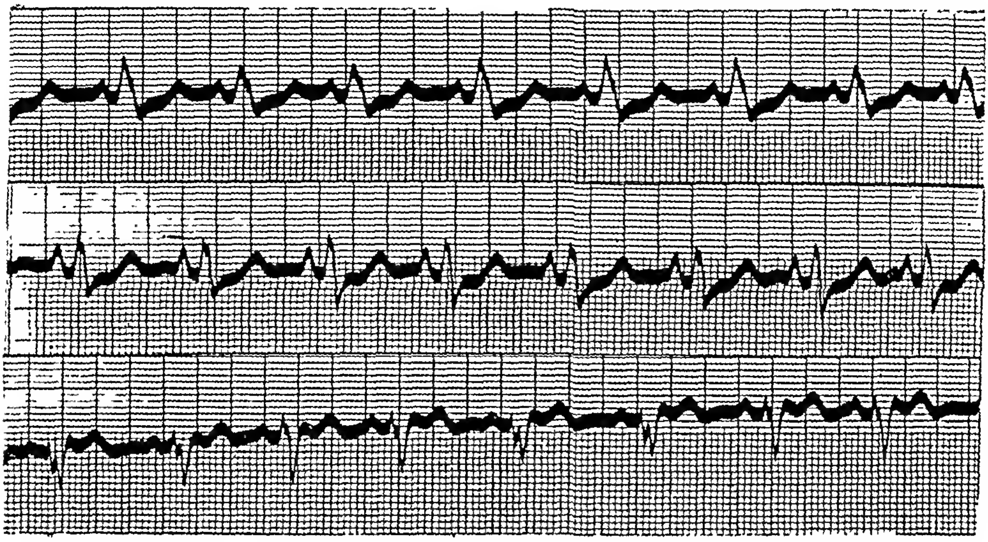

Fig. 1.—Case 1. Record on ninth day in the hospital. Normal mechanism. Marked splintering of ventricular complex with QRS interval of 0.14 second.

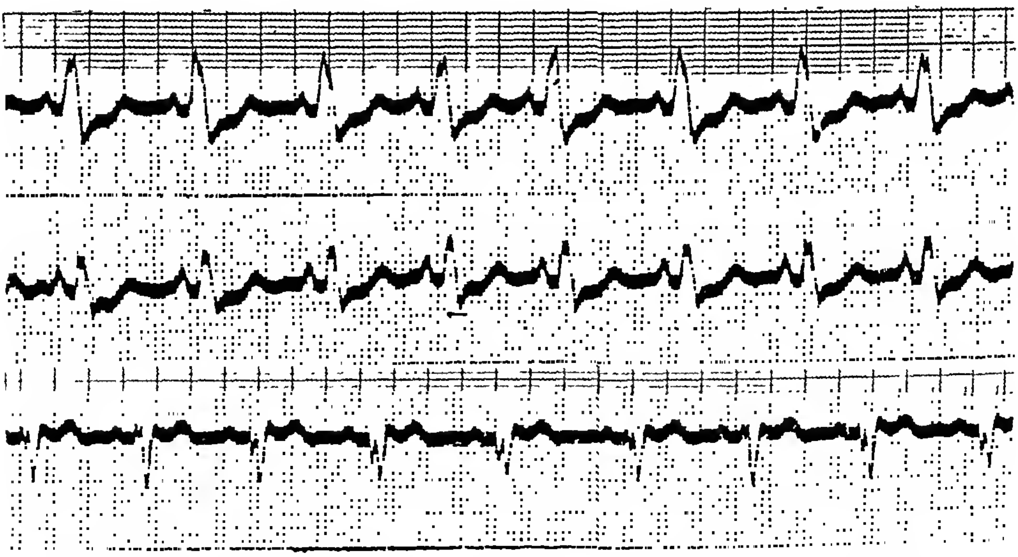

Fig. 2.—Case 1. Record on the following day, similar to the previous, but the excursions of Lead I are increased.

QRS has completely disappeared and the interval is reduced to from 0.10 to 0.12 second in all leads. Left ventricular preponderance is still marked (Fig. 3). The last record, taken on the fourteenth day, is normal. QRS interval is 0.08 second. Lead III is of low amplitude and T-waves are inverted here (Fig. 4).

Case 2.—A white girl, 6 years old, received 40,000 units of antitoxin after entering the hospital on the third day of the disease. She improved gradually and

was discharged after forty-five days in the hospital, with instructions to spend most of her time in bed for the next two weeks.

About the eighth day in the hospital her pulse fell to 60 where it remained until the twelfth day when it rose to about 100. An electrocardiogram taken on the eleventh day shows a rate of about 60 with a regular rhythm interrupted by auricular or nodal extrasystoles. This might be considered complete heart-block

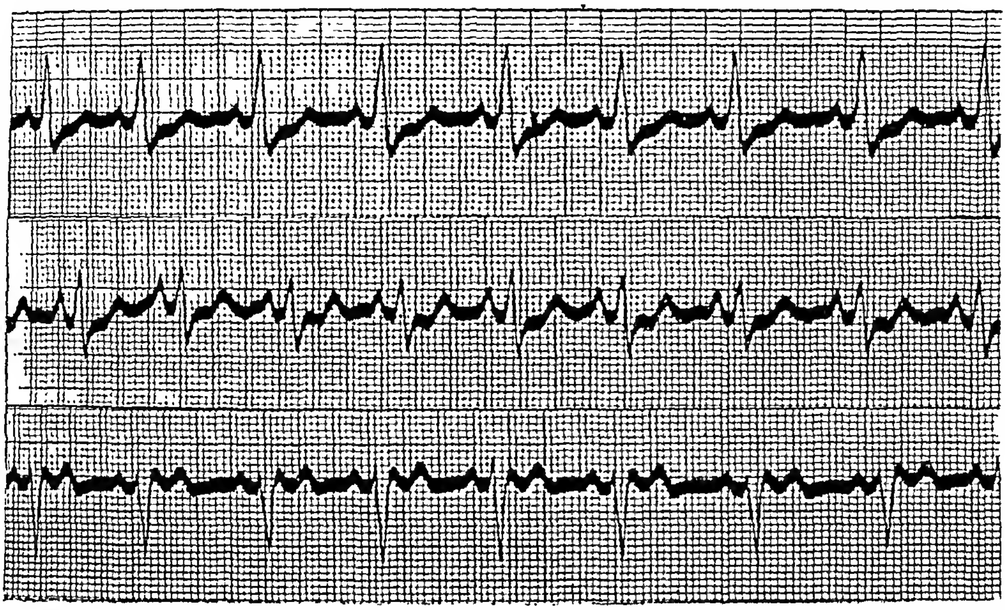

Fig. 3.—Case 1. Record on the eleventh day. Splintering of ventricular complexes has disappeared, and QRS interval is reduced to from 0.10 to 0.12 second.

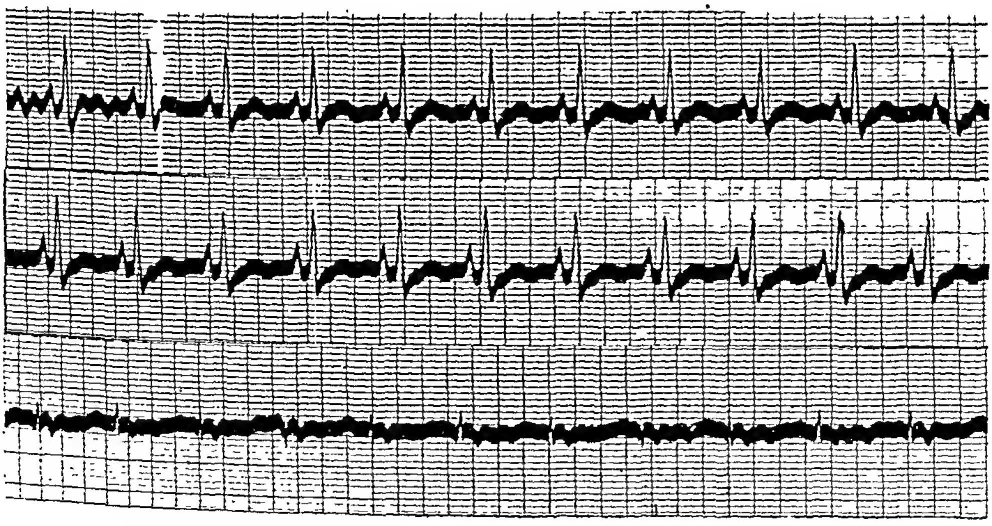

Fig. 4.—Case 1. Record on the fourteenth day is normal.

with independent ventricular rhythm, but the fifth complex of Lead I, the last complex of Lead II, and first, third, fifth and last complexes of Lead III definitely follow P-waves. Where ventricular action follows auricular contraction shortly after the preceding systole, the QRS complexes are smaller than usual but have the same general form as the others. QRS complexes in Leads II and III are diphasic and the interval varies from 0.14 to 0.16 second (Fig. 5).

A record taken three days later shows a normal mechanism except for auricular extrasystoles, the fourth complexes in Leads I and II. The P-R interval is normal, QRS complexes are upright and notched in all leads, and the interval is delayed to 0.12 second. The T-wave is constantly inverted (Fig. 6).

Five more records were made, all showing progressive improvement. The last record, made three days before discharge, shows a regular mechanism, normal P-R interval and normal QRS complexes except for low voltage. T-wave is inverted in Leads II and III (Fig. 7).

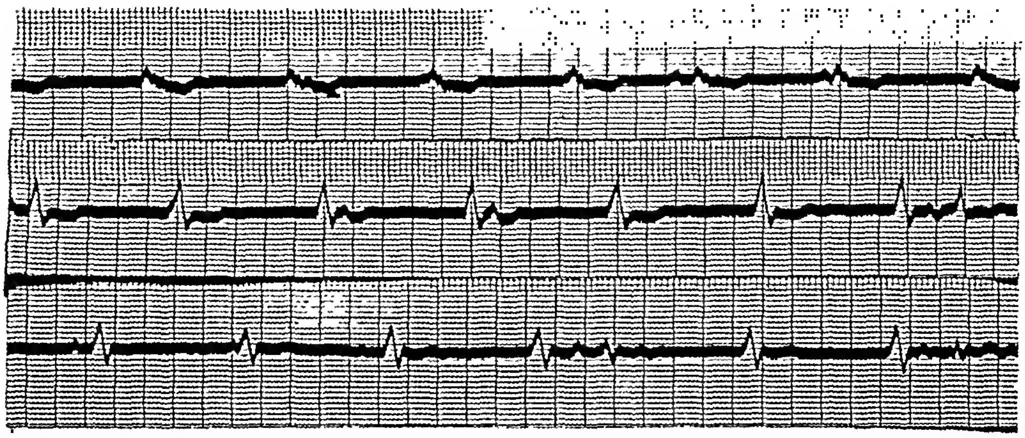

Fig. 5.—Case 2. Record on the eleventh day showing nodal rhythm with auricular extrasystoles. Marked widening of QRS complexes from 0.14 to 0.16 second.

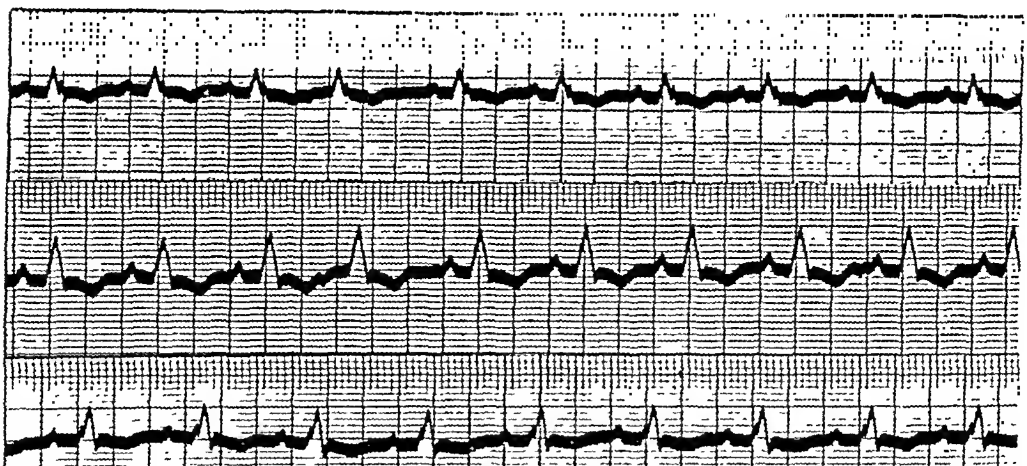

Fig. 6.—Case 2. Record on the fourteenth day shows splintering of venticular complexes with QRS interval of 0.12 second. The rhythm is regular except for isolated auricular extrasystoles in Leads I and II. T-wave is constantly inverted.

Case 3.—A white girl, 13 years old, received some injections into the buttocks from the family doctor on the sixth day of the disease and entered the hospital on the eighth day, receiving 2,000 units of antitoxin at that time. She improved steadily during her stay and was discharged with pharyngeal paralysis after thirty days in the hospital.

An electrocardiogram taken on the fifth day in the hospital shows a regular rhythm and rate of 70. The P-R interval is fully 0.2 second. QRS complexes

are notched in all leads, upright in Leads I and II and inverted in Lead III, and measure from 0.14 to 0.15 second. The T-waves are opposite in direction to the main ventricular complexes in Leads I and III. This record shows right bundle-branch block, though the excursions are not so great as are usually seen (Fig. 8).

A record two weeks later shows a marked change toward normal (Fig. 9).

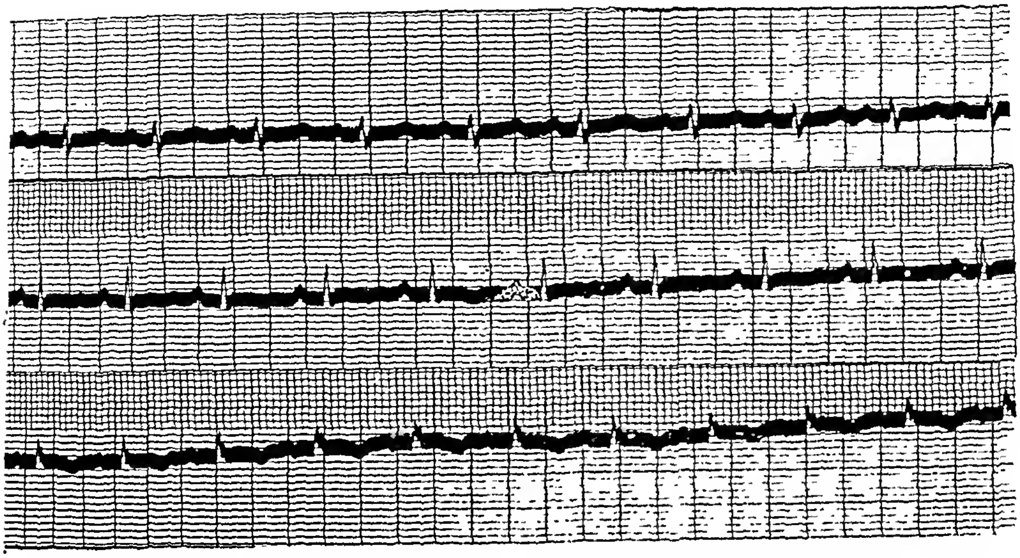

Fig. 7.—Case 2. Record before discharge from hospital. It is essentially normal except for low voltage and inverted T-waves in Leads II and III.

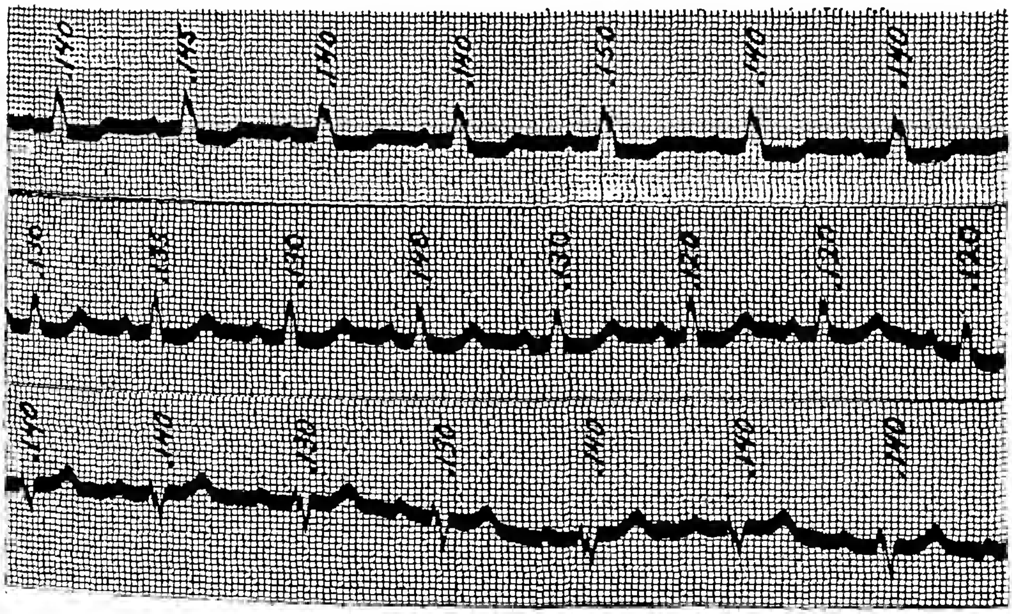

Fig. 8.—Case 3. Record on the fifth day showing splintering of ventricular complexes. QRS interval prolonged to 0.15 second and T-waves opposite in direction to that of main deflection. This record shows right bundle-branch block. P-R interval is 0.2 second.

CASE 4.—A white boy, 7 years old, received 40,000 units of antitoxin on admission to the hospital the fourth day of the disease. He was very ill with a pulse rate of 140 and blood pressure of 85/45 mm. He developed gallop rhythm and cardiac dilatation on the third day in the hospital, which persisted until the

twenty-eighth day. Improvement was progressive, however, and he was released on the thirty-first day to the care of his family physician with the understanding that he would remain in bed for two weeks.

The first electrocardiogram taken on the third hospital day reveals a regular rhythm with a rate of 120. The QRS complexes are upright, notched in all leads and show an interval of from 0.10 to 0.12 second. The T-waves are upright in

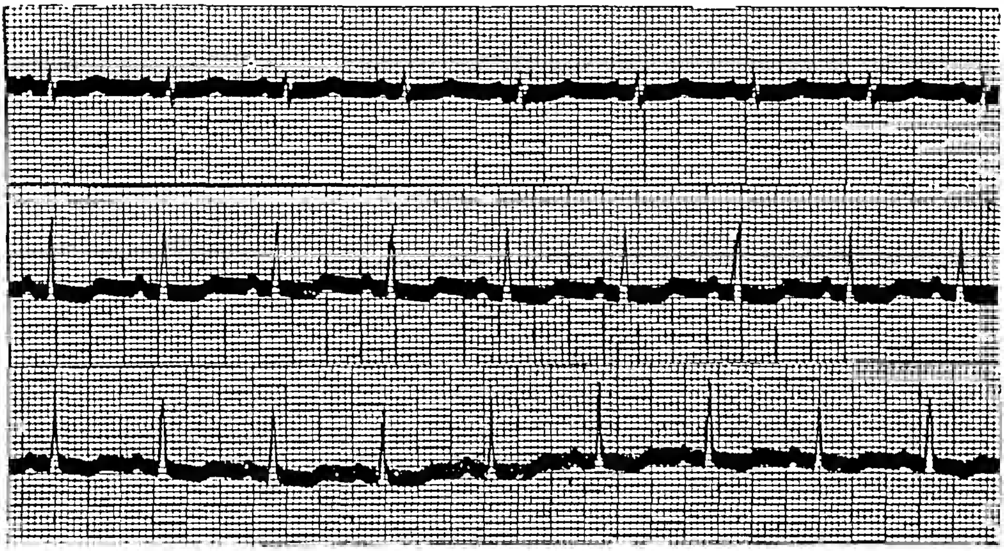

Fig. 9.—Case 3. Record taken two weeks later, which is essentially normal.

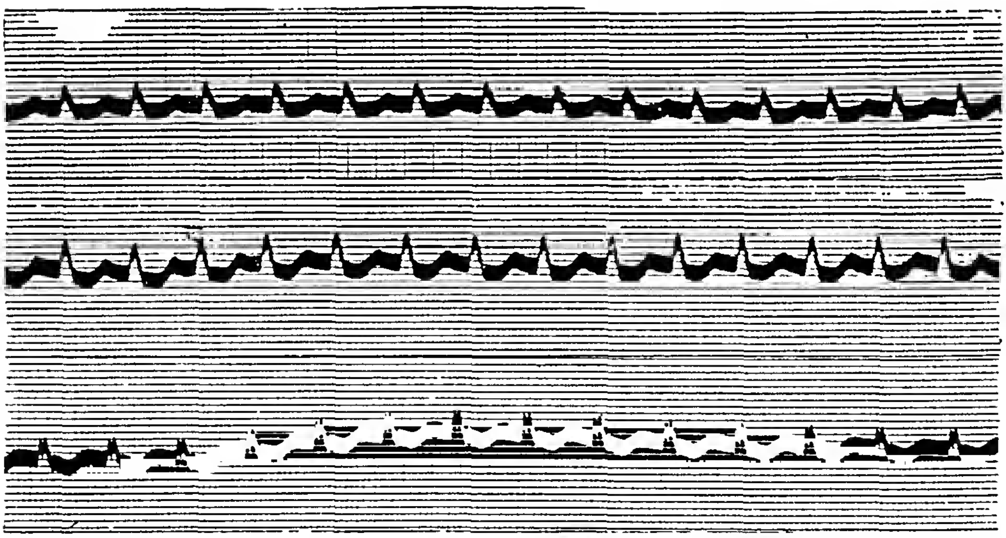

Fig. 10.—Case 4. Record on third day in the hospital shows ventricular complexes upright and splintered and QRS interval of from 0.10 to 0.12 second.

Leads I and II and inverted in Lead III. The voltage is low (Fig. 10). A record taken four days afterward shows notched QRS complexes with an interval of 0.12 second. These complexes are upright in Lead I and inverted in Leads II and III. The T-waves are opposite in direction to the initial ventricular complexes in all leads. The voltage is still low, otherwise the record suggests right bundle-branch block (Fig. 11). A record taken on the fifteenth hospital day shows notched

QRS complexes, but the interval has decreased to 0.08 to 0.10 second. They are upright in all leads but the voltage remains low (Fig. 12).

CASE 5.—A white girl, 7 years old, received 40,000 units of antitoxin on admission to the hospital on the fifth day of the disease. She was acutely ill; the blood pressure was low, and the pulse was feeble. There was no improvement in her condition, and on the fourteenth day she vomited, became cyanotic and pulseless, and died in a few hours.

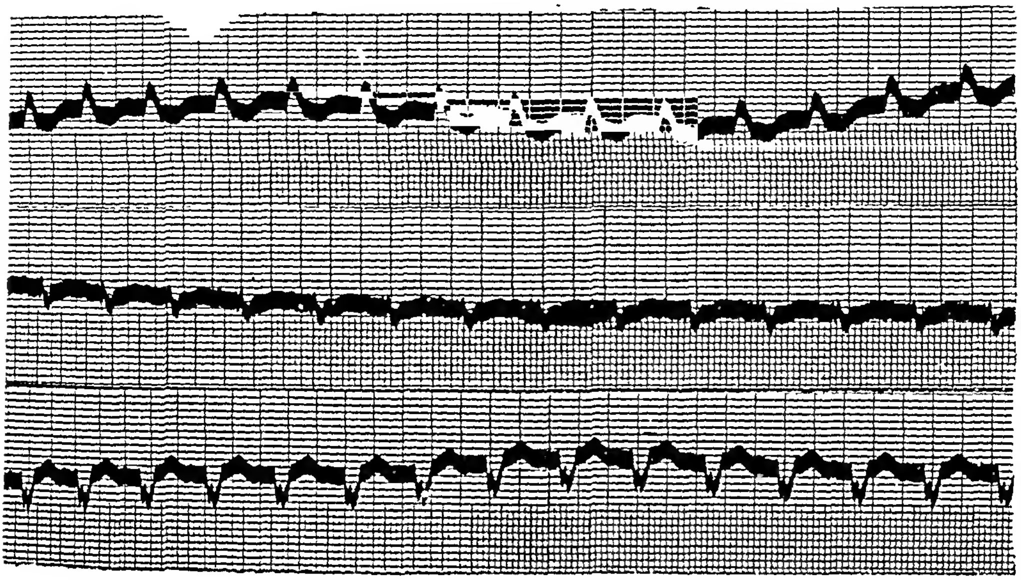

Fig. 11.—Case 4. Record four days later showing right bundle-branch block.

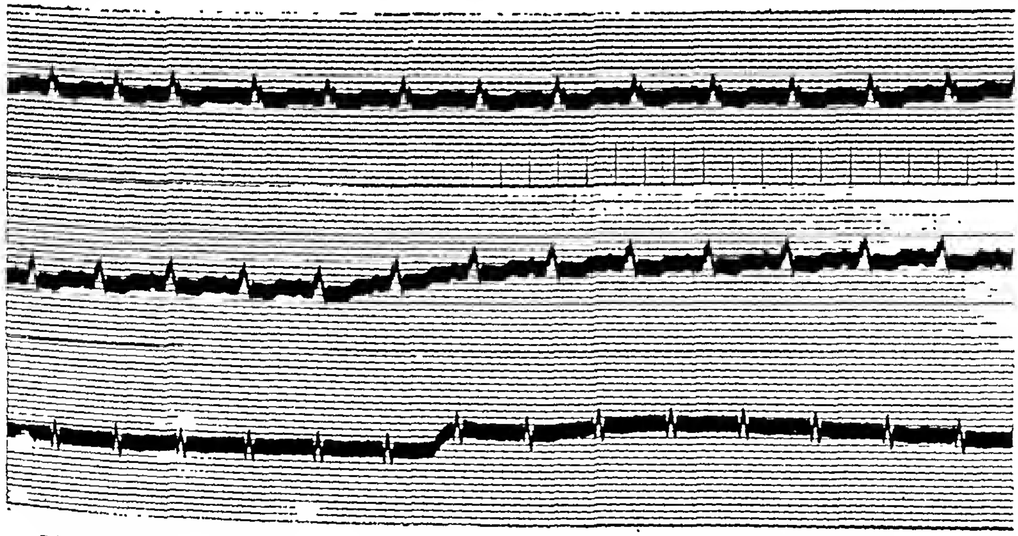

Fig. 12.—Case 4. Record on fifteenth hospital day showing definite change toward normal.

An electrocardiogram taken on the eleventh hospital day shows regular mechanism with a rate of 90. P-R interval is within normal limits. The QRS complexes are upright in Lead I and inverted in Leads II and III. The QRS complexes in Leads II and III are splintered, and the QRS interval is 0.14 second. The T-waves are opposite in direction to the initial ventricular complexes in all leads (Fig. 13). This record shows right bundle-branch block.

CASE 6.—A white girl, 10 years old, received 40,000 units of antitoxin on admission to the hospital on the seventh day of the disease. She experienced some difficulty in swallowing for several days due to swelling of the neck. The systolic blood pressure was consistently about 80 mm. and the diastolic varied from 0 to 40 mm. She seemed to be improving gradually, however, until the eighth day in the hospital when she suddenly collapsed and died.

Fig. 13.—Case 5. Record taken three days before death, showing splintering of ventricular complexes and delayed QRS interval of 0.14 second. This record shows right bundle-branch block.

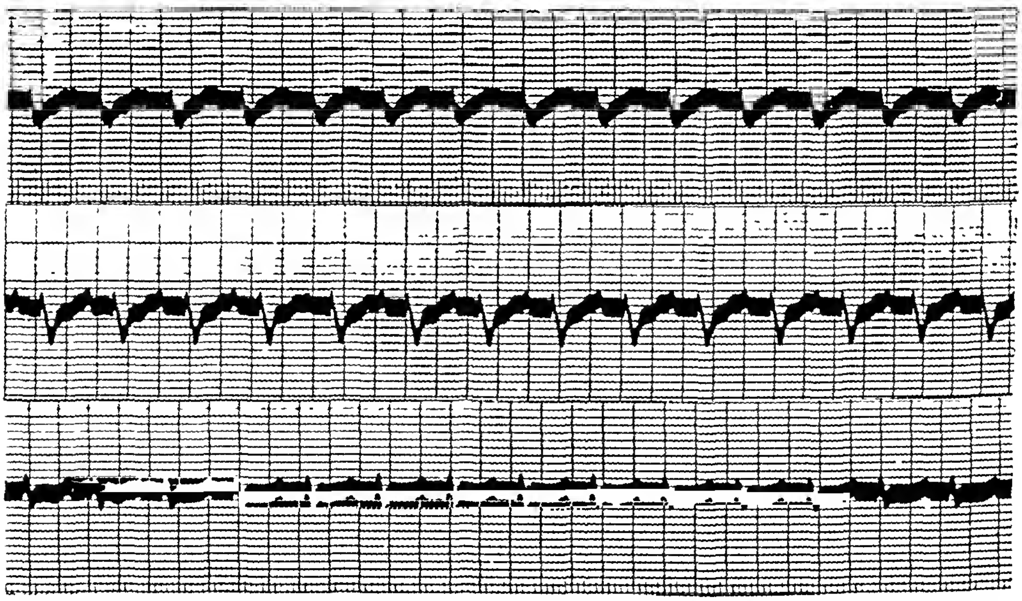

Fig. 14.—Case 6. Record taken the day before death shows inverted ventricular complexes in Leads I and II, delayed QRS interval, and indefinite T-waves.

An electrocardiogram taken on the seventh hospital day shows simple tachycardia, rate 128. The P-R interval is 0.2 second. The QRS complexes are inverted in Leads I and II; the amplitude is low and interval prolonged, though it is difficult to measure because it is indefinite. T-waves are also indefinite (Fig. 14).

DISCUSSION

The electrocardiograms from six cases of diphtheria are presented, showing delayed intraventricular conduction from 0.12 to 0.18 second. Definite notching of the QRS complexes is seen in each case. Cases 3, 4, and 5 (Figs. 8, 11, and 13) show right bundle-branch block. In the first, complete clinical and electrocardiographic recovery was observed; in the second, partial recovery was seen electrocardiographically and practically complete recovery clinically reported, while the third case terminated fatally. Case 1 suggests right bundle-branch block but is not typical because the T-wave in Lead 1 is upright. Cases 2 and 6 show marked intraventricular block. The QRS complexes are all upright with T-waves inverted in the first instance and voltage low and T-waves not definitely distinguishable in the latter instance.

The second case of this series showed an abnormal rhythm, which is interpreted as a nodal rhythm interrupted by auricular extrasystoles. Three days later normal P-R sequence was seen, and the rhythm was regular except for occasional auricular extrasystoles. Thereafter a regular mechanism prevailed until discharge. Normal mechanism was present in all the other cases. This might be explained by the fact that all cases associated with auriculo-ventricular block form the basis for another study and have been considered in the previous article.

Of the six cases studied, three were followed to electrocardiographic and clinical recovery. (The first case died of intercurrent infection after recovery from diphtheria.) One showed partial recovery before it was removed from our observation, and two terminated fatally at the height of electrocardiographic disturbance.

Intraventricular block is a group term suggested by Oppenheimer and Rothschild[2] to include arborization block and bundle-branch block, and is characterized by delay in the QRS interval. These authors reported a series of cases revealing at autopsy extensive fibrosis of the endocardial surfaces of the ventricles, which they called arborization block. The electrocardiograms showed delayed QRS conduction, low voltage, and absence of typical diphasic curves with large T-waves opposite in direction to that of the initial ventricular deflection of bundle-branch block. Bundle-branch block indicates a lesion of a branch of the conduction system below the bifurcation. The electrocardiograms under these circumstances show delayed QRS conduction with notching. The ventricular complexes are of large amplitude and diphasic with the T-wave opposite in direction to that of the initial deflection.

Numerous observers have reported delayed intraventricular block or bundle-branch block as transient phenomena. Robinson[3] has reported cases showing intraventricular conduction defects which disappeared with functional improvement of the heart. During the height of the disturbance and when the heart action was irregular, the beats follow-

ing long diastolic pauses were more nearly normal than those following short pauses. The element of rest and recovery in these cases, consequently, played an important part in conduction defects.

Willius and Keith[4] described three cases of incomplete bundle-branch block associated with myocardial disease. All showed a normal electrocardiogram with clinical recovery, so that the authors concluded that profound disturbances in ventricular conduction may be evanescent with or without cardiac decompensation. Leinbach and White[5] described a patient with a normal electrocardiogram and a slow rate at rest and right bundle-branch block during a rapid rate after exercise. Another patient showed alternate complexes of right bundle-branch block and normal mechanism before the branch block became permanent. Intraventricular conduction defects probably dependent upon functional depression were described by Wilson and Herrmann[6] in a case of uremia shortly before death. Colvin[7] described a similar case in carbon monoxide poisoning, followed by recovery.

The occurrence of intraventricular conduction defects in the course of diphtheria followed by electrocardiographic recovery, indicates that these phenomena may result from toxic depression of the conduction system.

SUMMARY

Six cases of diphtheria are presented in which delayed intraventricular conduction was observed. In four instances this was a transient phenomenon followed by electrocardiographic recovery.

The author wishes to express his appreciation to Dr. J. A. Toomey and the Department of Contagious Diseases for permission to study these cases.

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A COMPARISON OF RECORDS TAKEN WITH THE EINTHOVEN STRING GALVANOMETER AND THE AMPLIFIER-TYPE ELECTROCARDIOGRAPH*

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BOSTON, MASS.

DOCK[1] recently has reemphasized the distortion of the electrocardiogram which results from introducing a condenser in series with the leads from a patient to the string galvanometer and has made this phenomenon the premise for a critical analysis of records obtained with electrocardiographs of the resistance-and-capacitance-coupled amplifier type. He presents an illustration showing distortion of the S-wave, S-T interval, and T-wave produced by the amplifier-type instrument due to overshooting of the terminal part of the QRS deflection, and he states that this distortion increases with increase in dura-

Fig. 1.—A standardization record of the amplifier-type electrocardiograph.

tion and voltage of the QRS complex. Another illustration shows overshooting of the base line in the amplifier standardization record. In conclusion he states that although the distortion is slight in most records it must be considered in interpreting the tracings, and that electrocardiograms made in this manner can accurately duplicate Einthoven string galvanometer records only when the standardizing test current does not produce overshooting on the "break." For these reasons he considers the amplifier-type instrument unsatisfactory.

No other data on the accuracy of records obtained by electrical amplification of the heart currents are available. Because of this and the increasing popularity of the amplifier-type electrocardiograph, the Einthoven string galvanometer and amplifier records of twenty-five patients have been compared by detailed inspection and measurement. The amplifier-type instrument used was a late model of the Victor electrocardiograph, and the string galvanometer was a new Cambridge-Hindle model number two. The tracing on one instrument was taken immediately after that on the other, each apparatus being used first

*From the Research Laboratories, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School, Boston.

TABLE I

NAME	AGE	DIAGNOSIS	LEAD	RATE HINDLE	RATE VICTOR	P-R HINDLE	P-R VICTOR	QRS HINDLE	QRS VICTOR	Q-T HINDLE	Q-T VICTOR
			1	81	79	0.12	0.12	0.08	0.08	0.36	0.36
W.M.	17	Normal	2	77	77	0.12	0.12	0.09	0.09	0.36	0.37
			3	77	78	0.12	0.12	0.09	0.09	0.35	0.35
			1	66	66	0.16	0.17	0.08	0.08	0.37	0.38
W.R.	40	Normal	2	63	66	0.20	0.20	0.08	0.08	0.39	0.36
			3	66	64	0.19	0.20	0.09	0.09	0.36	0.36
			1	82	89	0.12	0.15	0.07	0.07	0.32	0.32
P.D.	20	Normal	2	82	86	0.14	0.14	0.10	0.09	0.34	0.35
			3	79	84	0.12	0.12	0.10	0.10	0.35	0.34
			1	87	91	0.15	0.15	0.08	0.08	0.32	0.32
C.M.	34	Normal	2	80	84	0.15	0.16	0.08	0.08	0.34	0.34
			3	77	87	0.15	0.15	0.08	0.08	0.33	†
			1	73	73	0.38	0.38	0.08	0.08	0.30	0.30
A.D.	28	Mitral stenosis	2	74	73	0.34	0.34	0.08	0.08	0.30	0.30
			3	74	74	0.32	0.32	0.08	0.08	0.32	0.32
			1	99	95	0.20	0.21	0.10	0.10	0.32	0.32
I.D.	15	Mitral stenosis	2	102	99	0.20	0.21	0.10	0.10	0.32	0.32
			3	96	102	0.20	0.21	0.10	0.09	0.33	0.32
			1	75	73	0.15	0.15	0.08	0.07	0.35	0.35
M.A.	27	Normal	2	77	77	0.16	0.16	0.08	0.08	0.35	0.35
			3	78	77	0.16	0.16	0.08	0.08	0.34	0.33
			1	49	50	0.16	0.16	0.08	0.08	0.41	0.41
A.E.	27	Normal	2	48	55	0.16	0.16	0.11	0.11	0.42	0.42
			3	46	48	0.16	0.16	0.12	0.12	0.42	0.42
			1	75	74	0.16	0.16	0.08	0.08	0.32	0.32
B.J.	24	Normal	2	80	72	0.14	0.14	0.09	0.09	0.36	0.36
			3	78	74	0.15	0.14	0.08	0.08	0.35	0.36
			1	60	61	0.14	0.14	0.12	0.12	0.36	0.36
S.E.	55	Normal	2	65	63	0.15	0.15	0.12	0.11	0.37	0.37
			3	62	60	0.15	0.15	0.11	0.11	0.37	0.37
			1	116	121	0.20	0.20	0.08	0.08	0.28	0.28
R.R.	24	Aortic regurgitation	2	121	125	0.19	0.19	0.10	0.09	0.30	0.30
		Mitral stenosis	3	116	121	0.20	0.20	0.10	0.09	0.31	0.30
			1	58	70	0.11	0.11	0.09	0.09	0.42	0.42
B.G.	50	Angina pectoris	2	60	62	0.12	0.12	0.10	0.10	0.44	0.44
			3	58	62	0.13	0.12	0.09	0.09	†	†
			1	68	67	0.13	0.14	0.11	0.10	†	†
S.G.	58	Angina pectoris	2	68	68	0.13	0.14	0.10	0.10	0.39	0.39
			3	70	70	†	†	0.10	0.10	0.38	0.39
			1	80	82	0.17	0.16	0.07	0.07	0.33	0.33
N.F.	38	Secondary anemia	2	81	81	0.17	0.17	0.09	0.08	0.33	0.32
			3	79	81	0.16	0.16	0.07	0.07	0.30	0.30
			1	80	81	0.20	0.21	0.07	0.07	0.30	0.30
S.S.	76	Aortic regurgitation	2	77	91	0.23	0.23	0.09	0.09	0.32	0.33
			3	72	73	0.22	0.22	0.09	0.09	†	†
			1	96	97	0.11	0.11	0.07	0.07	0.32	0.32
J.S.	42	Bronchiectasis	2	93	86	0.13	0.13	0.08	0.08	0.34	0.34
			3	87	97	0.13	0.13	0.08	0.08	†	†
			1	81	76	0.10	0.10	0.08	0.08	0.38	0.38
I.P.	44	Essential hypertension	2	81	81	0.12	0.13	0.06	0.06	0.38	0.38
			3	80	77	0.12	0.13	0.08	0.08	0.38	0.38
			1	79	79	0.15	0.14	0.07	0.08	0.32	0.32
M.S.	26	Normal	2	83	78	0.14	0.15	0.10	0.10	0.35	0.34
			3	81	75	0.14	0.14	0.10	0.10	0.34	0.34

TABLE I

Duration P		Amplitude P		Amplitude Q		Amplitude R		Amplitude S		Amplitude T	
Hindle	Victor	Hindle	Victor	Hindle	Victor	Hindle	Victor	Hindle	Victor	Hindle	Victor
0.09	0.08	0.7	0.6	0.0	0.0	5.5	1.3	3.5	2.7	1.8	1.7
0.10	0.09	2.2	1.8	2.3	2.0	20.0	16.5	1.1	3.0	1.5	3.5
0.09	0.09	1.5	1.3	3.5	3.0	19.2	15.5	3.0	1.8	2.0	1.8
0.08	0.08	1.0	0.9	0.2	0.2	7.7	6.0	1.5	1.2	2.3	2.0
0.12	0.12	1.5	1.3	0.1	0.1	8.8	7.3	3.5	2.8	2.8	2.4
0.08	0.08	0.7	0.7	1.8	1.3	1.7	1.7	2.2	2.0	0.5	0.5
0.07	0.08	1.1	1.0	0.0	0.0	6.0	5.2	0.2	0.2	2.8	2.0
0.09	0.10	1.3	1.0	0.0	0.0	7.8	6.3	5.0	1.3	1.5	3.5
0.08	0.07	*0.3 −0.5	*0.2 −0.5	0.7	0.8	1.7	1.3	5.0	4.3	1.7	1.1
0.08	0.08	0.8	0.7	0.4	0.6	9.0	8.0	0.7	0.2	2.5	1.8
0.09	0.10	1.6	1.5	1.0	1.0	10.0	9.0	0.8	0.8	2.5	2.0
0.09	0.09	0.8	0.8	0.3	0.5	4.2	3.0	0.2	0.2	0.3	†
0.12	0.12	1.9	1.6	0.1	0.1	1.8	4.2	7.0	5.0	1.0	0.9
0.11	0.11	*2.0 0.5	*1.8 0.5	1.0	1.0	9.0	9.0	2.2	2.0	1.3	1.2
0.10	0.10	−0.4	−0.4	3.0	2.5	11.6	10.2	0.3	0.3	0.3	0.3
0.08	0.09	0.8	0.9	0.0	0.0	8.0	7.0	1.2	1.0	1.3	1.3
0.12	0.12	1.5	1.2	0.0	0.0	18.8	17.3	0.0	0.0	1.5	1.5
0.08	0.08	0.5	0.5	1.0	1.0	12.0	12.0	0.0	0.0	0.3	0.3
0.08	0.09	1.2	0.9	1.0	1.0	8.8	6.4	1.0	0.7	4.0	2.0
0.09	0.09	2.0	1.5	0.6	0.5	12.2	10.7	1.8	1.7	1.0	3.3
0.09	0.09	1.2	1.0	0.7	0.7	4.8	1.5	1.0	1.0	1.5	1.5
0.08	0.08	0.8	0.7	0.0	0.0	6.0	4.7	0.5	0.1	3.2	2.7
0.09	0.09	1.0	0.9	1.5	1.3	17.3	15.0	1.9	1.3	5.4	4.3
†	†	†	†	1.5	1.2	12.5	11.0	1.2	1.0	2.2	1.6
0.10	0.10	0.9	0.8	0.0	0.9	3.7	3.1	2.7	2.7	2.8	2.4
0.10	0.10	1.3	1.1	0.8	1.0	16.0	15.0	1.6	1.3	5.8	5.2
0.08	†	0.8	0.5	1.0	0.9	16.0	11.6	0.0	0.0	3.0	2.8
0.06	0.06	0.3	0.1	3.0	2.5	7.5	7.2	4.0	3.3	3.3	3.2
0.09	0.09	2.0	1.6	1.0	1.0	12.0	10.0	3.0	2.5	6.0	5.5
0.09	0.09	1.7	1.2	0.0	0.0	6.0	5.5	1.7	2.0	3.4	2.7
0.11	0.11	2.0	1.8	2.0	1.8	12.0	10.8	0.0	0.0	1.0	1.0
0.12	0.12	3.2	2.7	0.2	0.2	15.0	13.0	0.3	0.3	1.6	1.4
0.11	0.11	1.2	1.2	1.0	0.7	13.3	12.0	8.0	7.3	0.8	0.8
0.06	0.06	0.8	0.8	0.1	0.4	1.2	1.2	1.2	1.1	1.1	1.1
0.09	0.09	0.8	0.8	0.6	0.8	5.8	5.7	1.8	1.7	1.5	1.4
0.06	0.06	0.2	0.2	0.2	0.2	1.8	1.7	0.7	0.7	0.3	0.3
0.10	0.09	1.0	1.0	2.4	2.2	12.2	11.8	1.1	1.3	*−1.0+0.4	*−1.0+0.4
0.10	0.10	1.2	1.2	1.8	4.1	1.0	3.3	2.7	2.3	*−1.0+0.3	*−1.0+0.3
†	†	†	†	0.0	0.0	0.0	0.0	9.0	9.0	−1.2	−1.2
0.10	0.10	1.2	1.0	0.0	0.0	7.1	7.0	0.5	0.5	1.7	1.7
0.10	0.10	1.3	1.1	0.3	0.3	9.1	9.2	0.0	0.0	1.2	1.0
0.10	0.10	0.4	0.4	1.0	1.0	3.6	3.0	0.0	0.0	0.5	0.5
0.08	†	0.6	0.7	0.0	0.0	9.0	7.2	0.0	0.0	1.3	1.2
0.09	0.10	1.5	1.3	0.0	0.0	6.3	6.2	6.0	5.0	1.2	1.2
0.07	0.07	0.8	0.8	0.0	0.0	3.6	3.0	13.0	11.2	−0.3	−0.3
0.08	0.08	1.3	1.1	0.2	0.2	9.5	9.0	0.0	0.0	1.5	1.5
0.10	0.10	1.5	1.2	0.0	0.0	6.2	7.0	1.0	0.8	1.8	1.8
0.07	0.07	0.6	0.5	1.8	4.8	1.0	1.0	0.6	1.0	†	†
0.06	0.06	1.1	1.3	3.0	3.0	19.0	18.6	0.0	0.0	2.7	2.0
0.08	0.08	1.3	1.2	1.0	0.8	10.0	10.0	0.0	0.0	1.9	2.0
0.08	0.08	*+0.8−0.7	*+0.7−0.7	0.0	0.0	2.3	2.2	11.0	13.7	−1.0	−1.0
0.06	0.06	0.4	0.1	0.0	0.0	4.0	3.5	1.8	1.3	2.4	2.4
0.09	0.09	1.3	1.3	0.2	0.2	11.0	10.0	1.0	3.3	5.2	5.2
0.09	0.09	1.2	1.2	0.0	0.0	8.0	7.0	3.0	2.5	3.2	3.0

*Diphasic Wave.
†Indistinct.

Table I.—Cont'd

Name	Age	Diagnosis	Lead	Rate Hindle	Rate Victor	P-R Hindle	P-R Victor	QRS Hindle	QRS Victor	Q-T Hindle	Q-T Victor
G.S.	22	Normal	1	76	68	0.15	0.15	0.09	0.09	0.32	0.33
			2	67	67	0.14	0.14	0.10	0.10	0.34	0.35
			3	82	78	0.14	0.14	0.10	0.10	0.34	0.35
J.L.	21	Normal	1	77	72	0.16	0.17	0.08	0.08	0.34	0.34
			2	76	71	0.17	0.17	0.09	0.08	0.35	0.35
			3	72	70	0.16	0.16	0.08	0.08	0.35	0.35
L.R.	22	Normal	1	86	77	0.16	0.16	0.09	0.08	0.34	0.34
			2	81	75	0.15	0.16	0.08	0.08	0.36	0.34
			3	82	77	0.16	0.16	0.08	0.08	0.35	0.35
J.O.	31	Normal	1	72	69	0.16	0.17	0.08	0.08	0.36	0.36
			2	68	64	0.15	0.15	0.08	0.08	0.38	0.38
			3	63	62	0.15	0.15	0.09	0.09	0.38	0.37
D.G.	27	Normal	1	68	73	0.14	0.13	0.09	0.09	0.36	0.36
			2	78	73	0.18	0.18	0.10	0.10	0.36	0.37
			3	71	78	0.18	0.18	0.11	0.10	0.36	0.35
K.D.	65	Normal	1	82	87	0.12	0.12	0.09	0.09	†	†
			2	82	87	0.12	0.12	0.08	0.08	0.34	0.34
			3	82	86	0.13	0.13	0.09	0.09	0.34	0.34
W.G.	46	Normal	1	86	82	0.14	0.14	0.08	0.08	0.34	0.34
			2	87	85	0.15	0.15	0.06	0.06	0.34	0.34
			3	88	86	0.14	0.14	0.08	0.08	0.31	0.31

†Indistinct.

on approximately one-half the patients. All records were made with the patient supine, and no change in position was allowed during the shift from one electrocardiograph to the other. Skin resistance, as measured with the comparison circuit of the string galvanometer, was in no instance over two thousand ohms at the time of taking the tracing with this instrument, and in no record was there overshooting of the string. Particular attention was given in all instances to accuracy of standardization. Measurements were made with the aid of a reading glass, and the amplitude of all waves was checked by superimposing the two records of each patient. In tracings showing variations in voltage of a wave the maximum amplitude of each wave was recorded. The results of the study are presented in Table I.

No difficulty was experienced with overshooting of the base line in the standardization records of the amplifier-type instrument. A typical standardization is shown in Fig. 1. The time relationships (P-R QRS and Q-T intervals) of the records obtained with the two electrocardiographs were practically identical throughout, and the amplifier tracings accurately duplicated all the finer details of waves recorded by the string galvanometer. In no instance did the amplifier records show overshooting of the terminal part of the QRS deflection with consequent distortion of the S-T interval and T-wave. Fig. 2 shows no overshooting of the QRS in a patient with waves of increased amplitude.

Amplitude of Deflections.—The measurements of height of the various waves showed small but distinct differences in the records obtained with the two instruments. In the majority of instances, however, the dif-

TABLE I.—CONT'D

DURATION P		AMPLITUDE P		AMPLITUDE Q		AMPLITUDE R		AMPLITUDE S		AMPLITUDE T	
HINDLE	VICTOR	HINDLE	VICTOR	HINDLE	VICTOR	HINDLE	VICTOR	HINDLE	VICTOR	HINDLE	VICTOR
0.09	0.09	0.3	0.3	0.0	0.0	5.2	5.0	1.0	0.8	2.0	2.0
0.10	0.10	1.3	1.2	1.4	1.3	12.8	12.8	1.5	1.3	3.7	3.7
0.09	0.09	1.2	1.0	1.4	1.3	10.6	10.0	1.6	1.0	2.2	2.2
0.08	0.08	1.0	0.8	0.1	0.1	10.0	8.2	2.5	2.1	3.6	3.4
0.09	0.09	1.6	1.3	3.0	2.6	20.8	18.2	0.0	0.0	5.0	4.6
0.08	0.09	1.0	0.9	2.8	2.3	13.2	12.2	0.0	0.0	1.9	1.4
0.08	0.08	0.9	0.8	1.0	0.7	9.0	7.2	1.0	1.0	2.3	2.3
0.09	0.09	1.3	1.0	0.3	0.3	9.0	8.2	1.3	1.0	3.4	3.4
0.08	0.08	0.8	0.8	0.0	0.0	2.5	1.7	1.7	2.0	1.3	1.3
0.09	0.10	1.2	0.9	0.0	0.0	6.7	5.7	8.0	7.0	2.7	2.2
0.09	0.09	2.0	1.7	0.5	0.5	9.7	9.0	0.7	0.5	4.8	4.5
0.09	0.09	−0.8	−0.8	2.2	2.0	13.8	13.2	0.0	0.0	2.7	2.2
0.06	0.06	1.0	0.9	0.5	0.5	8.2	7.0	0.8	0.3	3.4	2.7
0.11	0.10	2.0	1.8	0.0	0.0	7.2	5.5	3.0	2.4	4.5	3.4
0.08	0.08	1.6	1.4	0.0	0.0	1.3	1.1	2.2	2.0	1.2	1.2
0.08	0.08	1.4	1.4	1.4	1.2	9.7	9.2	0.0	0.0	0.2	0.3
0.07	0.07	1.3	1.1	0.0	0.0	7.8	7.2	4.2	4.2	3.2	3.0
0.08	0.08	*+0.4−0.7	*+0.4−0.7	0.0	0.0	4.0	3.7	6.5	6.2	4.0	3.0
0.08	0.08	1.0	1.0	0.0	0.0	11.8	11.8	0.5	0.5	2.0	2.0
0.09	0.09	1.3	1.2	0.0	0.0	9.2	8.0	0.2	0.2	3.0	2.8
0.08	0.08	0.5	0.6	0.0	0.0	0.0	0.0	3.0	4.0	1.3	1.0

*Diphasic wave.

ferences observed were of no practical significance. The P-waves in either two or three leads of the amplifier records of eighteen patients were slightly lower than in the string galvanometer tracings. The diminution in amplitude ranged from 0.1 to 0.5 mm. In over one-fourth of the leads the waves were of the same height, while in approximately one-half there was a diminution of 0.1 or 0.2 mm. The P-wave in one lead of four amplifier records was slightly higher than in the corresponding string galvanometer tracings. A large majority of the Q-waves were of the same amplitude in the two types of electrocardiograms, although with waves of rather large amplitude a diminution in the amplifier records amounting to as much as 0.5 mm. was observed. In two leads of one record and in a single lead of three others the Q-wave in the amplifier tracing was 0.1 or 0.2 mm. higher than in the string galvanometer curves. Differences in height of the R-waves ranging from zero to 3.7 mm. were observed, two-thirds of the amplifier leads showing diminutions of less than 1.1 mm. In only one lead of a single record was the R-wave higher in the amplifier than in the string galvanometer tracing. The S-waves of the amplifier records showed a diminution in height ranging from zero to 2 mm., there being no difference in over one-third of the leads and differences of 0.1 to 0.5 mm. in another one-third. In four tracings the S-wave of the amplifier records was higher in one lead than in the string galvanometer curves, the difference amounting to 0.3 to 1 mm. The T-waves in the amplifier records showed diminished amplitude ranging

from zero to 1.1 mm. with nearly one-half of the tracings showing a difference of zero or 0.1 mm. In one lead of two records, the T-wave of the amplifier curve was 0.1 mm. higher than in the string galvanometer tracing. Throughout the measurements of amplitude it was ob-

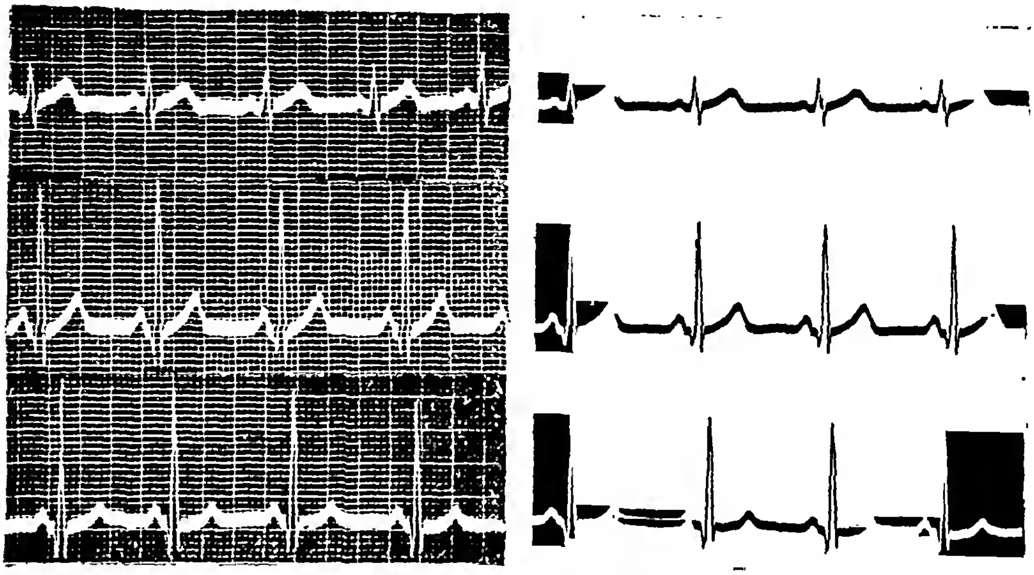

Fig. 2.—String galvanometer and amplifier electrocardiograms of a patient with waves of increased amplitude. Note absence of overshooting of terminal part of the QRS complex and accurate duplication of notching of descending limb of the R-wave in Lead I. All waves of the amplifier record are of diminished amplitude, the difference being most marked in the R-wave of Leads II and III.

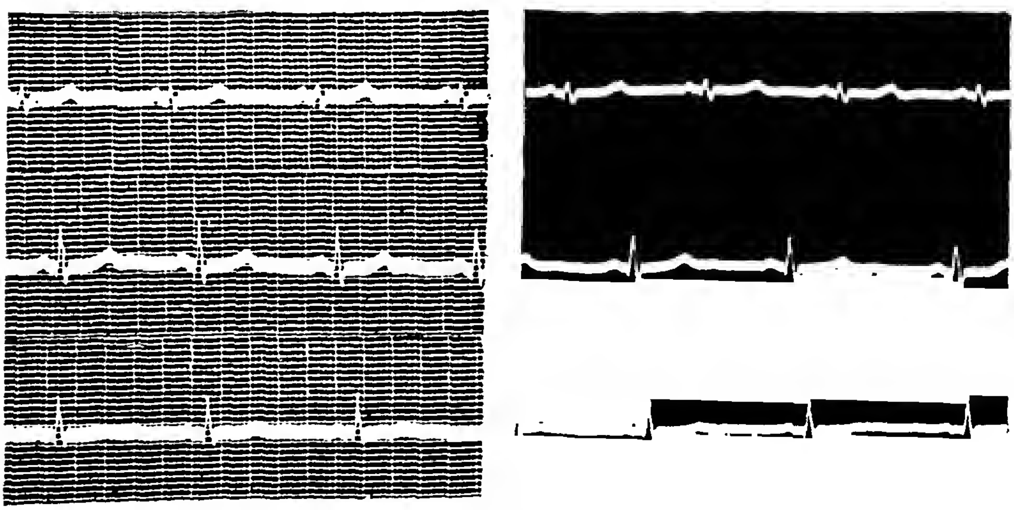

Fig. 3.—String galvanometer and amplifier electrocardiograms of low normal voltage showing practically no difference in height of any wave in the two records.

served that the differences in the two types of records tended to be greater in waves of higher voltage. Fig. 3 shows practically no difference in height of any wave in the two records of a patient with complexes of low normal voltage; while in Fig. 2, with waves of increased amplitude, the amplifier deflections are diminished.

CONCLUSIONS

The string galvanometer and amplifier-type electrocardiograms of twenty-five patients have been compared.

The time relationships and the finer details of all waves were accurately recorded by the amplifier-type instrument. No difficulty was experienced with overshooting of the base line of the standardization record or with overshooting of the terminal part of the QRS deflection.

With the exception of the Q-wave the deflections in the amplifier records were usually of slightly less amplitude than in the string galvanometer tracings. In all waves the difference in amplitude tended to be greater in complexes of higher voltage, but only occasionally did the difference assume a practically significant magnitude. No attempt was made to find a theoretical explanation for the differences observed.

Since the curves obtained with the amplifier-type instrument were essentially the same as those recorded by the string galvanometer, except for the slight differences in amplitude, they may be considered satisfactory.

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VEGETATIVE ENDOCARDITIS DUE TO THE BRUCELLA MELITENSIS*

WITH A CASE REPORT

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INTRODUCTION

WITHIN the past few years the medical literature of this country has been reporting increasing numbers of cases of undulant fever, more commonly designated as Malta fever. However, due to the low mortality rate of the disease in the United States, practically none of the reports include necropsy findings. This is in distinct contrast to European reports, particularly those from the Mediterranean countries, where the malady is more prevalent and of greater virulence. Then, too, in most of the cases of undulant fever now being reported in this country, the causative agent is the Brucella melitensis, variety abortus, or even the Brucella abortus (Bang) itself. However, in the goat-raising districts of the southwestern part of the United States, Malta fever due to the true melitensis species is endemic. The first epidemic of the malady that has ever been recorded in the United States occurred in that section of the country in 1922.[1] Most of the European cases are due to the Brucella melitensis, variety melitensis A, the organism found in the present case.[2]

In Carpenter's statistical report of 18 cases of undulant fever which occurred in New York State during the year ending June, 1927, 17 showed evidence of Br. abortus infection, while the remaining case, which incidentally is the present one, showed the Br. mellitensis A.[3] Evans, in a recent review of 20 cases of undulant fever reported in the United States, gave the abortus variety as the causative organism in all 20 instances.[4] In 1918 the same observer pointed out the very close biological and serological relationship between these organisms; in fact, so intimately are they related that they cannot be distinguished by ordinary laboratory tests.[4, 5] A slight but definite distinction between the two varieties may be detected by the agglutinin absorption test.

After a survey of the literature, we were unable to find recorded any fatal cases, with necropsy findings, of subacute bacterial endocarditis due to the Br. melitensis, variety melitensis A, in this country. In

*From the Third (New York University) Medical Division and the Pathological Laboratories, Bellevue Hospital, New York City. Read (in abstract) before the New York Pathological Society, Jan. 10, 1929, and published in the Archives of Pathology, May, 1929.

1926 Moore and Carpenter reported a fatal case of subacute bacterial endocarditis due to the Br. abortus from the Second (Cornell) Medical Service of Bellevue Hospital which at necropsy showed a vegetative endocarditis implanted on an old deformed aortic valve.[6] Recently Scott and Saphir reported a case of Br. melitensis, variety abortus, bacteremia associated with endocarditis. However, they stated that there was no proof in their case that the endocarditis was caused by the brucella infection.[7] They believed that their case was one of an acute and chronic endocarditis associated with Br. melitensis (abortus) bacteremia rather than one of endocarditis caused by the brucella itself.

In view of these facts, it seems justifiable to place on record the following case which was observed clinically and which came to necropsy.

REPORT OF CASE

T. G., a white male 38 years old, born in Italy, and a laborer by occupation, was admitted to Bellevue Hospital, Third (New York University) Medical Service, on December 8, 1926, complaining of fever.

Previous history.—His family history was irrelevant. The patient served in the Italian army during the World War, during which time he received typhoid inoculations. He did not recall having had any childhood diseases. In 1916 he had malaria. In 1917 swollen glands of the neck were removed. While in Italy in March, 1926, one month before he came to the United States, the patient drank goat's milk.

Present illness.—In May, 1926, one month after arrival in this country, the patient was admitted to a hospital in New York City where a diagnosis of influenzal pneumonia was made. This diagnosis was later changed to typhoid fever after a positive Widal test was obtained. During his stay in this hospital he had a persistent temperature, an enlarged liver, a palpable spleen, and a systolic murmur was heard at the apex. He left the hospital early in September, 1926, against the advice of the physicians and went to the country. After feeling well for about three weeks, the patient began to have daily attacks characterized by chills lasting about twenty minutes, fever of from one to five hours duration, which was accompanied by profuse perspiration, and severe headaches. Concomitantly with these symptoms he experienced a sharp, more or less continuous pain across the small of the back which radiated around both upper quadrants of the abdomen. Somewhat later the patient developed a similar pain in the left buttock, and the heel of the left foot. Three weeks prior to admission to Bellevue Hospital, or about the middle of November, the small toe of the right foot became very painful, and he noticed that it was turning black.

Physical examination.—On admission the patient appeared chronically ill and seemed to have lost weight. He was slightly dyspneic but not orthopneic, and had an anxious expression on his face. His skin had a slight café au lait tint. The pupils reacted to light and accommodation. The conjunctivae were slightly bluish. The fundi oculi were normal. Many bad teeth were present. Several petechiae were seen on the under surface of the tongue. There was readily visible a purpuric rash over both lower extremities, most marked above the ankles. The small toe of his right foot was reddened, with some blackish discoloration, swollen, and extremely tender to touch. Petechiae were present on the fourth toe, one being present as a splintering hemorrhage under the toenail. This toe was also extremely tender. Both feet were slightly edematous. His fingers presented a definite clubbing.

The veins of the neck were not dilated, but the carotid pulsations were somewhat exaggerated. A purpuric rash was visible on the anterior aspect of the chest wall. No substernal tenderness was elicited. There was an area of dullness at the left base with diminished fremitus, bronchovesicular breathing, increased voice sounds, and many moist râles. Infarction at the left lower lobe was considered. The apical beat of the heart was visible in the fourth space 9.5 cm. to the left of the median line which was just outside the midclavicular line. The first sound was of poor muscular quality. The pulmonic second sound was accentuated. There was present a distant, musical, systolic murmur, heard with maximum intensity at the apex and transmitted to the left. Another systolic murmur was heard at the aortic area. The rhythm was regular. The rate was 96. The systolic blood pressure was 90 mm.; diastolic 60 mm. The temperature was 101 degrees F. The spleen was palpable two fingers beneath the costal margin, with a firm, hard edge but not tender. The liver was palpable 10.5 cm. below the xiphoid and tender. No ascites was present.

Course.—During the patient's stay of approximately three weeks in the hospital, his temperature was irregular, not of the undulant type from which the disease received its name, and ranged from 99 to 104 degrees F. His pulse rate ranged between 80 and 120. Normal sinus rhythm prevailed throughout his illness.

Several days after admission, a tender, purplish-red spot was observed on the tip of the fourth finger of the right hand at the edge of the nail. This was interpreted as being an Osler's node. A week later this had disappeared, as had also the one on the fourth toe of the right foot. Some ecchymoses of the small toe of this foot were still visible, but the tenderness had disappeared.

X-ray examination of the chest on Dec. 13, five days after admission, revealed congestion at the right base adjacent to the heart, which organ was enlarged to right and left. On Dec. 29, three weeks after admission, the patient complained of pain in his right thigh anteriorly. Tenderness was not marked over this area, but the femoral pulse in this leg was scarcely palpable. Early in the morning of Dec. 31 the patient suddenly cried out with pain in his groins. This subsided by four o'clock under the effect of morphia. At 5 A.M. he complained of severe pain in the lower abdomen. His skin became cold and clammy. Death took place one hour later.

The clinical diagnosis was as follows: I. Malta fever (undulant fever); II cardiac disease; (a) bacterial, active, Br. melitensis A., (b) endocarditis, subacute, (c) regular sinus rhythm, (d) class 3.

Laboratory Data.—On admission the patient had 3,930,000 red blood cells with 48 per cent hemoglobin; the white blood cells numbered 3,350 with 69 per cent polymorphonuclear neutrophiles and 26 per cent lymphocytes. Twelve days later the count was 2,600,000 red cells with 55 per cent hemoglobin and 1,800 white cells with 66 per cent polymorphonuclears and 34 per cent lymphocytes. A few days before death the cell counts were about the same as the second one. The Wassermann was negative. The first urine examination revealed the following: dark amber, specific gravity 1016, acid reaction, one plus albumin, no glucose, many finely granular casts, moderate amount of pus and epithelial cells. An analysis two weeks later gave a similar result; close scrutiny failed to reveal the presence of red blood cells. The Mosenthal test showed fixation in the higher dilutions. The red test was 20 per cent in the first hour and 25 per cent in the second. Vital capacity readings averaged 1500 c.c. on four occasions. Electrocardiographic tracings were normal.

A blood culture taken the day following admission presented a growth of colonies four days later. The organism was identified as a very small gram-negative, nonmotile, bacterium, so small that its outline could not be clearly defined. This same organism was obtained a week later after five days of incubation, but the colonies

were much less numerous. These cultures, as well as serum obtained during life, were forwarded to Dr. Charles M. Carpenter of the Diagnostic Laboratory of the N. Y. State Veterinary College to whom we are greatly indebted for his very careful and detailed study. Dr. Carpenter reported the causative organism as being a true type of Brucella melitensis A.

Necropsy Report.—The body was that of an adult male, 165 cm. in length, of slender, well-developed frame, fairly good musculature and nutrition. The fingers were distinctly clubbed. The skin presented a tint distinctly comparable to that of café au lait. There were no petechial hemorrhages to be made out in the visible mucous membranes or in the skin, with the exception of the skin covering the under surface of the little toe of the right foot, where there were several brownish or reddish-brown, streak-like patches. In addition, there was a single splinter hemorrhage beneath the nail of the little toe and of the toe immediately next to it.

Fig. 1.—The two anterior aortic cusps are practically completely destroyed and replaced by a massive, friable vegetation. At about the center of the posterior cusp may be seen the remains of the small vegetation which broke off during necropsy.

On section, the subcutaneous fat and muscle tissues were well preserved and the peritoneum was smooth and glistening. The diaphragm was normally placed. The liver was distinctly enlarged, the lower edge reaching almost to the level of the umbilicus. The lower pole of the spleen projected beneath the costal slope on the left side for a distance of about 2 cm. Beneath the peritoneum in the right and lower portion of the abdomen was an enormous amount of bluish-red, apparently freshly clotted blood. The blood, on dissection, was found to occupy a space which could just about be covered by a large hand, extending from the right side of the lumbar spine outward and upward beneath the peritoneum to a point almost reaching the midline of the body anteriorly, and upward almost to the level of the lower border of the pancreas, and downward just to the level of the brim of the pelvis. The clot, on removal, weighed approximately 450 grams. Examina-

tion of the psoas magnus muscle failed to reveal any point of rupture and on section the muscle was not infiltrated by hemorrhage. At the same time, careful dissection of the mass, after removal, failed to show any sign of miliary aneurysm or any other anatomical cause for rupture.

Chest.—No thymic remains were visible. Both pleural cavities were fairly extensively obliterated by sheet-like adhesions which were broken down without great difficulty. The precordial area was large and the heart appeared to be floating. On opening the pericardium, fully 500 c.c. of perfectly clear straw-colored fluid escaped. The pericardium throughout was smooth and glistening.

Heart.—The heart appeared to be about normal in size. It weighed 345 gm. Both auriculoventricular openings were easily permeable, and the endocardium was excellently well preserved throughout, except for the two anterior aortic valves; these were practically completely destroyed and replaced by a solitary whitish or faintly cream-colored, granular mass of fused vegetations, irregularly round in shape, rather soft and friable, and approximating the size of one's thumb (Fig. 1).

Fig. 2.—The two anterior aortic cusps are practically completely destroyed and replaced by a massive, friable vegetation. At about the center of the posterior cusp may be seen the remains of the small vegetation which broke off during the necropsy. (Part of heart shown in Fig. 1, showing details.)

The mass served apparently to completely block the aortic orifice. The posterior aortic valve was distinctly thickened, white in color and glistening, and on the ventricular surface, at about its center, presented a pea-sized vegetation which was of the same general appearance as that already described. This vegetation, however, was loosely attached and fell away apparently of its own weight. The heart muscle was pinkish in color, opaque, but otherwise apparently well preserved. The aorta was excellently well preserved.

Lungs.—The left lung, except for the adhesions mentioned above, a moderate amount of anthracosis, and some edema of the upper lobe, was apparently normal. The right lung was essentially the same as the left.

Spleen.—The spleen was massive, weighing 1035 gm., and measured 20 x 14 x 5 cm. It was bound to the under surface of the diaphragm and to the peritoneum externally by fibrous adhesions which in places were string-like, in other places sheet-like, but all of them were broken down without great difficulty. On removal,

the spleen presented a bluish-red appearance, and at the extreme upper pole were two wedge-shaped, cream-colored bodies, which lay apparently flush with the surface, were firm in consistency and, on section, extended downward for a distance of about 2 cm., presenting a perfectly smooth, yellowish surface and a distinctly reddish periphery. On the outer surface of the spleen, at about its center, was a somewhat rounded body which was about one centimeter in length on the surface, and which, on section, presented essentially the same naked eye changes as the infarctions at the upper pole. The splenic substance was diffusely bluish-red in color, somewhat opaque, rather more friable than in ordinary circumstances, and presented, scattered over the cut surface, moderate numbers of minute whitish specks, suggesting focal necroses or abscesses.

Kidneys.—The left kidney measured 15 x 7 x 3.5 cm. It was imbedded in a moderate amount of fat.. The organ was distinctly enlarged, as indicated by its measurements; it cut without difficulty. The capsule stripped with ease and left behind an extensively and finely speckled surface. The speckling was due to the presence of numerous red points, between which the kidney substance showed as cream-colored islands, with here and there a pinpoint sized, sharply circumscribed, yellowish speck, corresponding apparently to miliary abscesses. The cortex bulged somewhat on section, and its markings were irregular. Scattered through the cortex were innumerable pinpoint sized red specks and moderate numbers of whitish or yellowish points, corresponding again, apparently, to abscesses. The right kidney measured 13 x 7 x 3.5 cm. and presented essentially the same naked-eye appearance as its fellow on the opposite side. The kidneys together weighed 530 gm.

Liver.—The liver was enormous, measuring 31 x 22 x 8 cm. and on removal weighed 2850 gm. Its surface was perfectly smooth, the capsule glistening. On section, the organ cut readily. The cut surface presented a pinkish background, scattered through which were numerous dull red specks, giving the organ as a whole a somewhat nutmeg appearance. Otherwise no focal lesions were visible in it. The substance was rather opaque, however, and a bit more friable than usual.

Lymph nodes.—Scattered throughout the retroperitoneal fat were moderate numbers of lymph nodes which varied in size from a few millimeters up to one centimeter. They appeared swollen and edematous, and presented a pinkish, opaque appearance. Some of them were finely speckled and occasionally one saw a minute white point, suggesting miliary abscesses.

The other organs were apparently normal on naked eye examination.

Anatomical Diagnosis.—1. Massive vegetative and ulcerative endocarditis of the aortic valves. 2. Massive septic splenomegaly with multiple anemic infarctions. 3. Subacute hemorrhagic nephritis. 4. Chronic parenchymatous degeneration of the liver. 5. Massive subperitoneal hemorrhage in right half of abdomen of unknown origin. 6. Subungual petechial hemorrhages in small toe and fourth toe of right foot. 7. Subcuticular hemorrhagic extravasations beneath the under surface of the right small toe.

Microscopic Examination.—Sections of the myocardium taken from various parts of both ventricles, presented slight lymphatic infiltration, consisting mainly of large and small round cells; no polymorphonuclear neutrophiles were seen. Moderate cloudy swelling and granular degeneration of the muscle fibers were also visible. A section through the large vegetation involving the right anterior aortic cusp showed a more or less homogeneous mass of granular and hyalinized material, fringed by a ragged edge from which pieces had apparently broken off. The base of the vegetation was directly continuous with the remains of the cusp, at which point organization had taken place. Gram-Weigert stain revealed no organisms in this massive vegetation.

The glomeruli of the kidneys showed beginning atrophy and infrequent hyalinization. Around some of them, within Bowman's capsule, were infiltrations of red blood cells and in many others infiltrations of small round cells around the capsules. A few presented moderately thickened Bowman's capsules. The tubules presented marked cloudy swelling and granular degeneration of the epithelium. An extravasation of red blood cells was visible in many of them. The arterial vessels were sclerotic and engorged.

Anthracosis and moderate congestion was seen in the lung sections.

The liver sections showed a marked degeneration around the central veins with pigment deposits; scattered islands of fat globules and a diffuse round cell infiltration were also visible.

Sections of the spleen presented marked congestion, scattered foci of necrosis, and a small area of anemic infarction.

COMMENT

The patient undoubtedly became infected in Italy by drinking goat's milk shortly before coming to the United States. The onset of his symptoms occurred about one month after his arrival, at which time he was admitted to a hospital where a diagnosis of influenzal pneumonia, which later was changed to typhoid fever, was made. In so far as both influenza and typhoid fever are two of a number of diseases which closely simulate undulant (Malta) fever, and because of the history of typhoid inoculations in the Italian army which might readily give a positive Widal reaction, the probability is that the fatal illness already manifested itself at that time.

The duration of the malady in this instance was, therefore, of about nine months simulating the subacute course of Streptococcus viridans endocarditis. Embolic phenomena as manifested by the petechiae and Osler's nodes, were obvious. The clubbing of the fingers, the enlarged spleen, and the café au lait tint of the skin completed the picture of a subacute bacterial endocarditis. Whether the endocardial lesion was the main seat of the disease might perhaps be questioned. However, it was the essential pathological lesion and undoubtedly caused by the Brucella melitensis.

The massive subperitoneal hemorrhage in the right half of the abdomen remains unexplained. The possibility of an embolic or mycotic aneurysm of a small peritoneal blood vessel which ruptured might be entertained, particularly in the presence of a large friable vegetation in the left side of the heart.

SUMMARY

A case of undulant (Malta) fever due to the Brucella melitensis, variety melitensis A, associated with a vegetative and ulcerative endocarditis of the aortic valves, and which clinically presented the manifestations of subacute bacterial (infective) endocarditis, is reported.

NOTE.—The necropsy was performed by Dr. Douglas Symmers, Director of Laboratories, to whom grateful acknowledgment is made for the courtesies extended.

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Department of Reviews and Abstracts

Selected Abstracts

Perla, David, and Deutch, Max: The Intimal Lesion of the Aorta in Rheumatic Infections. Am. J. Path. 5: 45, 1929.

Two instances of macroscopic involvement of the arota in recurrent rheumatic fever are described. A striking feature is the presence in one of the cases of an acute fibrinous lesion of the intima. The characteristics of the lesion are Aschoff bodies in the adventitia, perivascular infiltrations in the outer third of the media with destruction of elastic tissue and muscle elements, and recent and organized fibrinous plaques in the intima, the connective tissue cells comprising the vascular organization tissue having a characteristic vertical orientation at the base of the intimal lesions.

The authors believe that three groups of lesions may be distinguished in the aorta as the result of rheumatic fever. First, involvement of the adventitia tissues alone with perivascular infiltration and formation of Aschoff bodies. Second, involvement of the adventitia and the media. Third, involvement of all three layers of the arota in either an acute or chronic process.

Taussig, Helen B.: A Case of Bundle-Branch Block Confirmed by Pathological Study. Bull. Johns Hopkins Hosp. 45: 40, 1929.

A case is reported in which there was a long-standing chronic rheumatic infection with severe myocardial damage. The first definite evidence of left bundle-branch block occurred only a few days before death.

The author has found in the literature reports of only eleven cases of complete bundle-branch block and one case of transient bundle-branch block that have been followed up by careful pathological study. Histological examination of the heart after preservation in formalin in the present case showed extensive scarring of the left branch of the His bundle and a very slight actual break in the continuity of the bundle. The bundle-branch block probably developed as one of the late manifestations of a long-standing cardiac disease. The pathological findings were in apparent accord with the clinical observations.

McIntosh, Rustin: The Determination of the Circulating Blood Volume in Infants by the Carbon Monoxide Method. J. Clin. Investigation 7: 203, 1929.

The technic is described for the determination in infants of the circulating blood volume by the carbon monoxide method based on the successful use of this method in tests on adults. In comparison with the dye method, the carbon monoxide method gave results which were more uniform and showed a fair conformity with body weight.

In a small series of determinations of blood volume in patients less than two years of age, the correlation of blood volume, body weight to surface area and to body length suggested a normal interrelationship of these measurements. As an estimate of the circulating blood volume in infants exclusive of the newborn group, the formula

$$\text{Blood Volume in c.c.} = (\text{Body Weight in Kg.}) \times (77 \pm 13)$$

may be expected to give the correct figure in more than half the cases.

Lloyd, W. D. M.: Action of Calcium on the Isolated Human Fetal Heart. J. Pharmacol. & Exper. Therap. 36: 185, 1929.

The author has studied the action of calcium on two isolated human fetal hearts in perfusion experiments. As a result of addition of calcium salts to the perfusate, it was possible to show that there followed an increased strength of systole, a more regular rhythm, and better coordination between auricle and ventricle. At the end of one and one-half hours of perfusion all heart action finally ceased in systole of the ventricle.

Moon, R. O.: Some Observations on Diseases of the Myocardium. Brit. M. J., July 6, 1929, p. 1.

In this broad discussion of diseases of the myocardium the author presents the conventional views held on this subject. He divides the common types of myocardial disease into those due to fatty infiltration, fatty degeneration, fibroid heart muscle changes, and coronary obstruction. He discusses the diagnoses of patients with latent myocardial disease as well as those cases showing cardiac insufficiency. He indicates in series several points in the establishment of such a diagnosis. Under treatment the effect of climate, diet, and exercise are discussed.

McMillan, Thomas M., and Wolferth, Charles C.: An Untoward Effect of Barium Chloride in Producing Short Runs of Aberrant Ventricular Beats. J. Lab. & Clin. Med. 14: 839, 1929.

A case is reported in which during six years of observation the patient had four attacks of complete A-V heart-block lasting for varying lengths of time up to two months. During the third attack barium chloride may have been a factor in restoring the sinus rhythm and preventing the onset of complete block again for eight months. During the fourth attack of complete block which lasted four months and ended in death, barium chloride failed to increase the effective ventricular rate in doses of 20 mg. four times a day and for four days. This dosage of the drug brought on a marked extrasystolic disturbance with frequent short runs of rapid ventricular tachycardia.

The disturbance is reported because the authors regard it as potentially serious and an untoward result of barium chloride and because the drug previously has been regarded as harmless in much larger doses than was required to bring about the disturbance in this case.

Master, Arthur M., and Oppenheimer, Enid Tribe: Obesity. J. A. M. A. 92: 1652, 1929.

The authors have studied a series of 91 females and 8 males from an obesity clinic. The patients varied in age from ten to fifty-eight years, the greatest number being between thirty-five and fifty. The great majority did not have any ailments other than obesity. Blood pressures and pulse rates were studied at each visit, and in order to test the functional capacity of the circulatory system, a simple exercise tolerance test was also used.

The authors have noted that the obese person usually complains of dyspnea, fatigue, palpitation, dizziness, and headache. Sixty-seven per cent of the cases showed hypertension, and accelerated pulse rate was commonly present. In general, the more the overweight the greater the hypertension. With loss of weight the symptoms tend to disappear, and there is a corresponding fall in blood pressure

and pulse rate. With advancing years the blood pressure of obese patients increases. Apparently the longer the duration of the obese condition the higher the blood pressure.

Under thirty-three years of age the obese are somewhat more efficient than the average, suggesting that a moderate overweight in the young is a slight advantage.

The roentgenogram showed a sthenic or hypersthenic chest elevation of the diaphragm and an enlarged, widened heart with a hypertrophied ventricle and a hazy lower left border obscured by apical pericardial fat. With reduction in weight these characteristic signs disappear.

The electrocardiogram showed in 87 per cent a left ventricular preponderance. There was also noted a change in the P- and T-waves of the third lead. Sinus arrhythmia was common in this group of cases, occurring almost as frequently as ventricular preponderance.

The authors believe that it is clear from these studies that there exists in the obese person a distinct circulatory embarrassment, as proved by the abnormalities of the blood pressure, pulse rate, roentgenogram and electrocardiogram, and by the diminished capacity for work. It is not difficult to understand why the fat person is a poor surgical risk and why his mortality in pneumonia, nephritis, and heart disease is higher than the average. These factors give ample explanation for the distinct improvement commonly observed on reduction in weight in patients with valvular disease of the heart, hypertension, and coronary artery disease.

Bachmann, Harrold A.: Clinical Types of Edema in the Heart Failure of Childhood. Arch. Int. Med. 43: 795, 1929.

The author distinguishes two types of edema in children with cardiac disease. The first type is the commonly recognized dependent type involving the dependent portions of the body almost exclusively. It appears more prominently in the lower extremities, about the sacrum, and occasionally in other portions of the body. With this type of edema there is usually found ascites, marked enlargement of the liver, and other evidence of cardiac failure. As a rule, these children not only suffer from their discomfort and cardiac embarrassment but are also acutely ill and frequently toxic.

The second type of edema is generalized and corresponds to that seen in nephritis. It appears first in the face and later becomes equally prominent in all portions of the body. In degree it is never so overwhelming as that seen in nephrosis, but it has the same generalized distribution regardless of the position of the patient. Otherwise, the clinical picture is that of a patient with heart failure, though the heart failure is seldom so severe as that found in the previous type, nor is the patient ever so acutely ill. He appears more as a convalescent patient who has outlived an acute infection and presents the usually associated pallor and poor nutrition.

Response to treatment has shown a certain specificity which is of clinical value. In the dependent type of edema digitalis is of value while the addition of the milder diuretics aids little in hastening reabsorption and elimination. In the generalized type of edema, theobromine sodiosalicylate acts almost as a specific and usually without the aid of digitalis.

The type of lesion of the heart seems to influence little the kind of edema produced. It appears, however, that in the children whose history of heart failure is of recent date and whose hearts are, perhaps, still acutely infected, the edema associated with failure is more likely to be generalized. Dependent edema occurs almost exclusively in the patients with more chronic heart disease.

The prognosis of the patient with generalized edema is good, at least as to the immediate future, while that of the patient with the dependent type of edema is relatively bad.

Herxheimer, H.: Study of Heart Size in Olympic Athletes. Klin. Wchnschr. 8: 402, 1929.

In an x-ray of the heart size of Olympic participators the author comes to the conclusion that the endurance sports, such as long distance running, bicycling, and skiing, all cause a definite heart enlargement in proportion to the body weight of the individual.

Danielopolu, D.: Control of an Attack of Angina Pectoris by Pressure Upon Carotid Sinus. Klin. Wchnschr. 8: 596, 1929.

The author cites a case in which pressure upon the carotid sinus brought to an end an attack of angina pectoris. He believes that angina pectoris is precipitated by a pressor reflex, originating from "reflexogenic zones" in the heart, aorta, or carotid sinus and ending over the sympathetic pathway. By pressure upon the carotid sinus, it is possible that the same reflexogenic zone may originate a depressor reflex, ending over the parasympathetic pathway and thus bringing to an end the anginal attack.

Winternitz, M., and Selye, H.: A Case of Sinus Bradycardia Due to Arterial Thrombosis. Wien. Arch. f. inn. Med. 16: 377, 1929.

In a patient sixty-two years of age, with generalized atherosclerosis and uremia, a terminal bradycardia (43-47 beats per minute) occurred. Serial sections of the heart revealed an old obliterating thrombus in the artery supplying the sino-auricular node.

MacMahon, H. E., and Burkhardt, E. A.: Meningococcus Endocarditis. Am. J. Path. 5: 197, 1929.

A case of meningococcus endocarditis is reported with autopsy and bacteriological findings. The patient was a white woman, twenty-eight years old. The authors point out that it is important to remember that endocarditis can be caused by the meningococcus without any meningeal involvement and that such cases have been diagnosed as acute rheumatic fever with endocarditis or subacute bacterial endocarditis. They point out that the vegetations on the valve are rather typical, being large, firm, localized, and fungating with little tendency to discharge minute emboli. They believe that these organisms should be agglutinated and in some cases agglutinin absorption tests were performed in order properly to identify the meningococci. The literature pertaining to this subject is reviewed.

Hyland, C. M.: Meningococcus Endocarditis. J. A. M. A. 92: 1412, 1929.

The meningococcus may be responsible for extrameningeal lesions and that these lesions need not necessarily be associated with infection of the meninges has been known for some years. The author reports the case of a man, aged forty-six, admitted to the hospital with shortness of breath, excessive perspiration, and cough. There was fever, signs of heart disease, leucocytosis, and positive blood cultures showing meningococci. The patient died twelve hours after admission. Vegetations were found on the aortic valve at autopsy.

Gold, Harry, and DeGraff, Arthur C.: Studies on Digitalis in Ambulatory Cardiac Patients. J. A. M. A. 92: 1421, 1929.

It is shown in a study of patients that the therapeutic effects of digitalis may be induced in many cases by the daily repetition of such doses of the drug as the patient may eliminate daily after having been fully digitalized.

There has been included in this study also a note as to the behavior of digitalis in children as compared with adults. The authors have noted that the drug is less often seen to produce striking improvement in children because the type of heart failure relieved most effectively by digitalis is relatively common in heart disease among adults but relatively rare in children. In those cases in which less definite therapeutic effects are obtained, insufficient or excessive digitalization is more apt to occur because of the absence of a satisfactory guide to the intensity of digitalis action.

Cahan, Jacob M.: The Incidence of Heart Disease in School Children: J. A. M. A. 92: 1576, 1929.

This report is based on the examination of 10,333 pupils in seven elementary schools, two junior high schools, and one senior high school for boys of Philadelphia. The purpose of the survey was to investigate the incidence, the morbidity, and the prophylaxis of organic heart disease in the children of these public schools. The total enrollment in the school was 11,578. Nine hundred and forty-three children who showed definite or suspicious signs of organic heart disease were reexamined. At this time the child's cardiac history was obtained. Fifty-eight were studied in the hospital or cardiac clinic. The number of patients with heart disease was 94, or 0.91 per cent; of this number 51 were boys, 43, girls.

The younger children had a slightly lower incidence of heart disease than the older pupils. Valvular disease, mitral stenosis, was the most frequent lesion found. This anatomic diagnosis was made in 53 of the 94 children with heart disease. Fourteen of these 53 showed signs of mitral stenosis and mitral insufficiency.

Consideration was given to three additional factors bearing on the prevalence of heart disease in school children; namely, (1) children with grave heart lesions unable to attend school; (2) children with crippled hearts attending special classes, and (3) children with definite or suspicious heart lesions that are being overlooked because of the inadequate routine examination of the clothed chest.

Rentschler, Edwin B., Vanzant, Francis R., and Rowntree, Leonard G.: Arthritic Pain in Relation to Changes in Weather. J. A. M. A. 92: 1995, 1929.

This study was undertaken not to prove the relationship of arthritic pain to weather change but to determine whether or not such a relationship actually exists. In a group of 367 patients studied for a year, there was a positive relationship for 72 per cent of the time between the curve of pain and that of barometric pressure. For 21 per cent of the time the relation was equally definite, but as one line went up the other went down. In only 7 per cent of the time was a relationship undemonstrable.

For more than 90 per cent of the time there was a relation between the presence of storms and an increase of pain. Observations on humidity, temperature, and atmospheric electricity were inconclusive, although it is still possible that these agents working together have some effect.

The authors believe that many of the patients with arthritis can, with the increase of the severity of their pain, sense the approach or presence of storms. While this study has been confined to a group of patients with chronic arthritis, it is of importance in the study of climatic conditions in their relationship to rheumatism in general.

Yater, Wallace M.: Pathologic Changes in Auricular Fibrillation and in Allied Arrhythmias. Arch. Int. Med., **43:** 808, 1929.

A series of 145 cases of auricular fibrillation, 7 cases of auricular flutter, and 2 cases of paroxysmal tachycardia—all with necropsies—were studied from the stand-

point of etiology and pathology. All the usual types of heart disease were found, but cases of endocarditis and hyperthyroid states were the most numerous. Hypertension was found to be a common condition, but the occurrence of auricular fibrillation in other types of heart disease was uncommon. In about 8 per cent of the cases of auricular fibrillation, there was a combination of possible etiological factors and in about 9 per cent an etiological factor could not be suggested.

Twenty-nine hearts which had been the seat of these arrhythmias were studied microscopically. A distinctive lesion for the arrhythmia was not found and the lesions were not considered in themselves of sufficient importance to account for the arrhythmia. There apparently is not, therefore, a specific histological syndrome in auricular fibrillation and probably none in auricular flutter and paroxysmal tachycardia.

Rosenbluth, E., and Winterberg, H.: Blocking in a Case of Paroxysmal Supraventricular Extrasystoles. Wien. Arch. f. inn. Med. **16:** 333, 1929.

In a case of paroxysmal attacks of extrasystoles of supraventricular origin, the authors believe in accordance with Kaufmann's parasystolic theory, that the extrasystoles are due to the rhythmic activity of a center adjoining the sino-auricular node. Under ordinary conditions, the sinus exerts a blocking influence over this secondary center but when the excitability of the ectopic center becomes high enough, the extrasystolic mechanism comes into play. A case is reported with electrocardiographic findings.

Scherf, D., and Zdansky, E.: Influence of Atropine, Adrenalin and Amyl Nitrite on the Size of the Heart. Wien. Arch. f. inn. Med. **16:** 399, 1929.

The authors make use of a device called a roentgenkymograph to study the right and left heart borders in systole and diastole. This apparatus consists of an x-ray film which slides on two lead plates leaving slits which are placed over the heart borders after fluoroscopy.

By means of tracings thus made, they were able to determine that atropine, adrenalin, and amyl nitrite all caused a diminution in the systolic and diastolic diameters, the diminution being in proportion to the increase in pulse rate. The diminution of the heart size with adrenalin is explained by a predominating inotropic action which exceeds the tendency of the increased blood pressure to cause cardiac dilatation.

Redisch, W., and Rosler, H.: Studies of Capillaries in Congenital Heart Disease. Wien. Arch. f. inn. Med. **16:** 463, 1929.

The authors believe that the cyanosis in congenital heart disease is due, not only to the polycythemia and abnormally large amount of reduced hemoglobin but also to the peculiar capillary structure, consisting of numerous arched and winding loops with wide venous limbs. The sluggishness of the capillary stream is a marked feature.

Hurwitz, Samuel H., and Levitin, Joseph: The Value of Phenylhydrazine in the Treatment of Polycythemia Vera. Am. J. M. Sc. **177:** 309, 1929.

The purpose of this report is to record the clinical course of the patient with polycythemia vera treated with phenylhydrazine and to emphasize the value and dangers of this drug as well as the importance of certain criteria for the control of its dosage.

The patient was a woman 42 years old and under observation for two years. Splenomegaly was very slight if present at all. Hematuria was present and had caused her to be treated for Bright's disease. There was a transient palsy of the right arm. This may have been caused by a vascular lesion of the brain due to the formation of a small thrombosis. These patients show a great tendency to venous thrombosis.

Phenylhydrazine hydrochloride produced definite clinical improvement in the patient. The authors concluded that the drug is worthy of being given a trial if the dangers of its use be kept in mind. Guided by frequent counts of the red and white blood corpuscles and by estimations of the serum bilirubin, one may give phenylhydrazine without danger to the patient. It is wise to stop its administration before the red blood count reaches a normal level because its action continues after its withdrawal. The hemolytic crisis observed in these patients may be avoided if additional safeguards be used. Because of the great difference in the response of patients to varying amounts of the drug, quantitative determinations of the serum bilirubin and frequent leucocyte counts should be made. A marked rise in the amount of serum bilirubin means excessive blood destruction, whereas a rising leucocyte count probably indicates great destruction of liver cells.

Finally, it may be stated that the use of phenylhydrazine is no exception to the general observation that the various measures used in the treatment of polycythemia vera are transitory and that the effect produced is purely palliative. General experience seems to show that no matter what therapeutic measure is adopted there is a tendency for the red blood cell count to rise and for the subjective symptoms to return.

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